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Psychological development of infants conceived through in vitro fertilization

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PSYCHOLOGICAL DEVELOPMENT OF INFANTS CONCEIVED THROUGH IN VITRO FERTILIZATION

A Dissertation

Presented to

The Faculty of The School of Education

The College of William and Mary in Virginia

Williamsburg, Virginia

In partial fulfillment

of the requirements for the Degree

Doctor of Education

by

Virginia Lee Van de Water

July 1988

PSYCHOLOGICAL DEVELOPMENT OF INFANTS CONCEIVED THROUGH IN VITRO FERTILIZATION

by

Virginia Lee Van de Water

Approved July 1988 by

Roger Ries, Ph.D.

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John Lavach, Ed.D.
Chairman of Doctoral Committee

DEDICATION

To Drs. Howard and Georgeanna Jones

without whom there would have been
no study, and

without whom there would have been
no Thomas or Lee Van de Water.

ABSTRACT

In 1984, The National Institute of Child Health and Human Development awarded a grant to The Eastern Virginia Medical School and The Children's Hospital of The King's Daughters to study the IVF children conceived at The Jones Institute for Reproductive Medicine in Norfolk, Virginia. The purpose of the study was to assess the children comprehensively using a multi-disciplinary team to determine whether the IVF process resulted in higher than average physical and/or behavioral deficits. The children were psychologically tested on the Bayley Scales of Infant Development; they also received pediatric, neurological, cardiac, and ultrasound examinations of their internal organs. 83 of 105 eligible IVF children were examined. These children were matched on the following criteria: maternal age, child's age, race, gender, births/pregnancy, and socioeconomic status. The controls were obtained from a 100 mile radius of Norfolk, Virginia. Ninety-three children served as controls. All were between 12 and 30 months of age.

The results indicate that these families are different from the general population in several respects: they are older, better educated, more affluent, almost all white, and have a higher rate of multiple births. The groups did not differ in their rate of congenital defects. While

prematurity was common, the children demonstrated no adverse effects from their prematurity.

The psychological results indicated that both groups were above the national norms for the Bayley Scales on both their MDIs and PDIs; they did not differ significantly, but the IVF group was higher on both scores. Two IVF children with physical handicaps were cognitively normal. Behaviorally the groups did not differ at the p=.01 level on any of the Behavioral Record variables.

The NICHHD study concludes that the risk of the IVF process is acceptable from a medical viewpoint. The children who are born do not demonstrate a higher rate of physical or psychological abnormalities based on current information.

ACKNOWLEDGEMENTS

I wish to express my appreciation to John Lavach, Ed.D., my advisor, and to Roger Ries, Ph.D. and Michael Politano, Ph.D. who also served on my committee for their guidance.

A special thank you to my husband, Malcolm, who thought this was a good idea and who spent hours upon hours watching our children while I pursued this degree. Without his good-natured support it would not have been possible.

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JUSTIFICATION

In 1978, the first child was born as a result of in vitro fertilization in England (Sokoloff, 1987). Her birth represented an important breakthrough in the treatment of infertility, especially for women with blocked or missing Fallopian tubes. This process occurs in vitro, or in a glass petri dish, and it is properly referred to as IVF or IVF/ET (in vitro fertilization/embryo transplant). With the development of this procedure it became possible for physicians to supervise and manipulate the fertilization process outside the woman's reproductive tract in the laboratory. It allowed technology to bypass the mother's diseased or missing reproductive organs as well as the father's infertility. As of January 1988, Raymond in The Journal of The American Medical Association (JAMA) reports that the IVF technique has now resulted in 3,000 children being born worldwide to couples who probably would have been childless. The IVF children represent a new population, and one that will probably be increasing as the fertility rate declines in the U.S. (Goldman, 1988; Wegman, 1987).

Long before the process resulted in a birth, there were those who feared that children conceived in vitro would be at

risk for malformations and/or retardation (Kass, 1972). Behrman and Patton (1988) write that it has been widely held by "authoritative individuals" (p. 2) that infertile couples are endocrinologically disturbed and are likely to produce endocrinologically disturbed children as evidenced by more prematurity, more cesarean section deliveries, more fetal anomolies, and inferior offspring. These claims were made without "solid data" according to Behrman and Patton. Recognizing this as a concern, The National Institute of Child Health and Human Development (NICHHD) authorized a study in 1984 to investigate the health and physical condition of the IVF children born in the United States. The grant was awarded to Eastern Virginia Medical School and The Children's Hospital of The King's Daughters in Norfolk, Virginia, and the IVF children to be studied were the offspring of the IVF program at The Jones Institute for Reproductive Medicine in Norfolk. The research design was a combined effort of individuals from all three organizations. Data collection began in 1985 and ended in 1987. Andrews et al. (1986) referred to this study as a multidisciplinary diagnostic evaluation and neurodevelopmental assessment wherein the children are being "intensively evaluated" (p. 851). The results, as yet unpublished by Morin et al., indicated that there were no significant differences between the IVF children and their matched controls in their physical condition or psychological development during early childhood. The medical community and the consuming public

have needed this information to make the appropriate decisions because the IVF technique results in life itself. Sokoloff (1988) points out in an article addressing all non-coital reproductive methods, "There continues to be, however, a paucity of information on the well-being of the child produced by alternative reproduction techniques. How is he/she doing physically and emotionally?" (p. 11).

This research was a more detailed analysis of the psychological development of these children. It investigated the mental, motor, and behavioral characteristics of the IVF children and their matched controls. It investigated these factors relative to the general population and previously identified risk factors.

STATEMENT OF THE PROBLEM

The problem was to determine whether the IVF children are psychologically different from normally conceived children. For this study the infant's psychological development is defined as mental and motor development along with behavioral characteristics. The research questions are as follows:

1. Are there differences between IVF infants and matched controls on the mental and motor scales of the Bayley Scales of Infant Development?

2. Are there differences between IVF infants and normative data of the Bayley Scales?

3. Are there differences between IVF infants and controls associated with risk factors such as prematurity and multiple births?

4. Are there differences between IVF infants and controls on behavioral indicators?

THEORETICAL RATIONALE

The theoretical rationale for this research is based on Piaget's developmental theory as described by Piaget in Carmichael's Manual of Child Psychology (1970). When assisting Binet in 1904 in the development of Binet's intelligence test, Piaget recognized that the children's errors followed patterns and did not occur at random. His research and theorizing resulted in the identification of stages of development which are considered invariant and universal even though there are individual differences in how they are accomplished. For the early childhood years he identifies two stages. The first is sensori-motor which lasts until eighteen to twenty-four months of age. During this time the child develops object constancy, increasingly coordinated motor movements, and problem solving skills. Motor control progresses from the reflexive to the voluntary. The second stage begins with the onset of verbal language. Language provides the child with the symbols for conceptual intelligence. Memory and classification rely on symbolic

representation which is a prerequisite for adult intelligence.

Piaget published extensively in his lifetime on his observations and theories. In 1947 in Psychology of Intelligence he stated, "...behaviour becomes more 'intelligent' as the pathways between the subject and the objects on which it acts cease to be simple and become progressively more complex" (p. 10). He goes on to say:

> To define intelligence in terms of the progressive reversibility of the mobile structures which it forms is therefore to repeat, in different words, that intelligence constitutes the state of equilibrium towards which tend all the successive adaptations of a sensori-motor and cognitive nature, as well as all assimilatory and accomodatory interactions between the organism and the new environment (1947, p. 11).

Intelligence is regarded as a duality; it is seen as a process and as an ultimate goal. Intelligence-ultimate goal is a recognition that the adult is "more intelligent" than the child; there is constant comparison of the child's problem solving with that of the adult. Intelligence - adaptation is a biological process, a type of organic activity. In 1952 Piaget wrote in The Origins of Intelligence in Children, "In one sense and at the beginning of mental evolution, intellectual adaptation is thus more restricted than biological adaptation, but in extending the latter, the former goes infinitely beyond it" (p. 4).

Piaget theorized that intellectual development proceeds in stages. Furth (1969) identifies the criteria for a stage as follows:

1. Each stage involves a period of formulation (genesis) and a period of attainment. Attainment is characterized by the progressive organization of a composite structure of mental operations.

2. Each structure consititutes at the same time the attainment of one stage and the starting point of the next stage, of a new evolutionary process.

3. The order of succession of the stages is constant. Ages of attainment can vary within certain limits as a function of factors such as motivation, exercise, and cultural milieu.

4. The transition from an earlier to a later stage follows a law of implication analogous to the process of integration, preceding structures becoming a part of later structures (p. 27).

In short, there is an invariant sequence of intellectual development, and all humans proceed through these steps in the same way with some individual variation. The focus was on the universality of development.

Piaget concurs that there are some classical factors involved in development which he describes in Carmichael's Manual of Child Psychology (1970, p.719-20). The first of these is physical maturation. The second is experience of the physical environment through exercise and manipulation.

The third is the social environment; progress through the stages can be accelerated or retarded by the quality of the child's social situation. He asserts, however, that

> experience of the physical environment and social environment cannot account for the sequential character of development and the first (maturation) one is not sufficient by itself because the development of intelligence does not include a hereditary programming factor like the ones underlying instincts. ... Thus the effects of maturation consist essentially of opening new possibilities for development, that is, giving access to structures which could not be evolved before these possibilities were offered. But between possibility and actualization, there must intervene a set of other factors such as exercise, experience, and social interaction (1970, p. 720).

He postulates that there is a fourth factor which organizes the others. This is based upon the biological fact that development is a self-regulatory process, and he labels this fourth factor as equilibration. He considers this fourth factor to be the most important due to its organizing properties.

Equilibration is maintained by two opposing functions which he labels assimilation and accomodation. Cowan (1978) describes the equilibration model of intellectual functioning this way:

> ... it is a shorthand summary of the only two possible

> ways in which an organism can function in relation to an environment; it can modify the environment to fit its needs and structures (assimilation), or it can modify itself in response to environmental demands (accomodation) (p. 21).

It is important that the process be understood to be one of "controlled tension" and not as a resting state. When the balance is disturbed there is an opportunity to advance to a higher level. Advancement can occur when there is tension and conflict. Infancy is seen as a period of constant disequilibration until the development of symbolic representation. This is a period of rapid cognitive gains, and Piaget labeled it as the sensori-motor period.

This research assessed whether in vitro babies proceed through the same developmental stages as their regularly conceived peers. It has determined that the medical manipulations of the mother's hormonal levels and the exposure to laboratory conditions do not adversely affect these infants so that their intellectual development, motor development or behavioral characteristics are different from and/or inferior to their "normal" peers. The Bayley Scales of Infant Development require the infant to perform a series of increasingly complex tasks to evaluate their progress through the universal and invariate sequence described by Piaget.

DEFINITION OF TERMS

In vitro fertilization

In vitro fertilization refers to the process of stimulating production of multiple eggs through hormone therapy, retreiving the eggs when they are mature, and fertilizing them in a petri dish with the sperm. The fertilized eggs are then implanted into the woman's uterus in order that one or more will implant and mature into a fetus and eventually result in a live birth. This is undertaken for couples who have been unable to conceive through normal intercourse or more traditional treatments for infertility. It is now a "suitable treatment for a variety of causes of infertility" (Jones, 1988, p. 543) including tubal disease, semen abnormalities, immunological inferility, hostile mucus, and idiopathic infertility. The Norfolk program at The Jones Institute requires the following: a generally healthy husband and wife, accessible ovaries, normally functioning uterus, normal or correctable menstrual function, under age of 40 years, and uncorrected reproductive problem described above (Jones, 1988, p. 544). An important and now standard feature of the process is the variety of drugs used to stimulate egg production. These include clomiphene citrate, human menopausal gonadotropin (HMG), and follicle-stimulating hormone (FSH) individually or in combination. The ideal number of eggs is five or six which usually results in three or four actually being fertilized and implanted. After the eggs are retrieved they are incubated for 24 to 36 hours

before implantation. The sperm are washed at least three times before fertilization to initiate capacitation. Fertilization can be determined 14 to 18 hours after insemination. Under normal (in vivo) circumstances the fertilized egg reaches the uterus in 5 to 6 days, but the IVF process has been documented to slow cell division for unknown reasons. Consequently, the transfer of the fertilized eggs to the uterus is usually made on the third day following the retreival of the eggs. It is the practice of The Jones Institute to support the luteal phase of the cycle (after implantation) with progesterone administered intramuscularly daily. Whether this is necessary is undocumented (Jones, 1988). "After an IVF pregnancy is established, there is absolutely no evidence to indicate that it differs in any way from normal in vivo pregnancies", and no special monitoring activities are indicated (Jones, 1988, p. 557). There is a high rate of cesarean section following IVF, but Jones asserts that this is due to such factors as prior infertility surgery or obstetrical factors that contribute to the risk for a vaginal delivery. "The abortion rate following IVF compares very favorably with that following in vivo conceptions" (Jones, 1988, p. 557). During 1984, 17 of the 74 pregnancies resulted in multiple pregnancies, or 23%. Jones believes that twins and triplets are obstetrically and socially acceptable but larger numbers are not. They are associated with increasing risk for both mother and child,

and they present "difficult social problems for couples who planned a much smaller family" (1988, p. 559).

Mental and Psychomotor Index

The Mental Development Index (MDI) and Psychomotor Development Index (PDI) are standardized scores used in reporting the results of the Bayley Mental and Motor Scales. They have a mean of 100 and a standard deviation of 16 (Bayley, 1969). They are not to be interpreted as IQ scores, only as an indication of a child's performance relative to other children of the same age.

Socioeconomic status

Socioeconomic status is based in this research on the parental education. This does not always correlate with the financial status of the family, but as Bayley stated in 1937 "higher educational level is associated with higher occupational status, higher income, and higher socioeconomic rating as to home and neighborhood" (p. 333). It also has the advantage of being easily determined and avoids the reluctance of many people to divulge their income. In this same research Bayley discovered the mid-parent education to be the most highly related to mental scores. No such relationship was found between SES and motor development. In this study the mean parental education was the measure selected for analysis, but family income was requested and obtained from many participants.

Teratology

Teratology is the study of abnormal development. Its purpose is to understand the

> causes and mechanisms of maldevelopment. A teratogen is a substance, organism, or physical agent capable of causing abnormal development. A teratogen can cause abnormalities of structure or function, growth retardation, or death of the organism. ... There is growing interest in exploring the role of prenatal factors in more subtle or difficult-to-ascertain effects, such as growth retardation and developmental and behavioral abnormalities. A major area of current interest is behavioral teratology (Mortensen et al., 1986, p. 185).

It is the study of birth defects, and this study was designed to assess the possible teratogenic effects of the IVF process to include the psychological/behavioral effects.

RESEARCH HYPOTHESIS

The research hypothesis is that there will be no difference between the IVF subjects and their matched controls on congenital defects, mental development, motor development, or behavioral characteristics.

SAMPLE DESCRIPTION

The cases for this study were children born following in vitro fertilization at The Howard and Georgeanna Jones Institute for Reproductive Medicine in Norfolk, Virginia. They all had birthdates between October, 1983, and September, 1985. They were all between 12 and 30 months of age chronologically when evaluated. All children born during that time period were eligible to participate in the research. These children were born to a geographically diverse set of parents. The controls, however, were selected from the civilian obstetrical population within one hundred miles of Norfolk. The matching was done by an epidemiologist using hospital records from fifteen area hospitals. All professionals conducting the study were blind as to the child's status as a case or control.

PSYCHOLOGICAL PROCEDURES

The procedure for collecting the psychological data was the administration of the Bayley Scales of Infant Development in their entirety by the same examiner. Every effort was made to obtain the child's cooperation, and this was usually accomplished if the child was seen by the school psychologist as the first procedure of the day. A parent was present for the administration. The Behavior Rating Scale was completed immediately following the administration of the Mental and Motor Scales.

LIMITATIONS OF THE STUDY

This research was based on the children conceived at The Jones Institute in Norfolk, Virginia. While the parents came from all over the United States and some foreign countries. this was not a randomized sample. Likewise, the control group was selected from a one hundred mile radius around Norfolk, Virginia. These results may not be generalizable beyond those populations.

These children were all thirty months of age or younger. Long-term follow-up would be necessary to determine whether any trends identified hold up over time. Mental and motor development in infancy is well known to be a poor predictor of the child's ultimate mental or motor functioning. Behaviorally children may change over time, and the behavioral characteristics of the infant may be different from those of the same child as a teenager.

This study examined only live births and the possible associated defects. Teratology associated with mortality was beyond the scope of this study, but mortality figures would be important in assessing the overall safety of the IVF procedure.

ETHICAL CONSIDERATIONS

The families were fully informed as to the nature and purpose of the study. Each family, whether case or control, was fully apprised of their right to voluntary participation and withdrawl in the consent form (Appendix A). They were

assured that their child or family would not be identified in any way without their consent. All of the procedures were non-invasive and without risk based on current medical knowledge. The families were informed as to all findings relative to their child. The child's pediatrician received a copy of all findings and recommendations if any were considered necessary. The parents were also advised as to how to obtain a copy of the results when the study is complete.

CHAPTER 2

RATIONALE AND PROBLEM

The Piagetian concept of universal and invariate developmental stages enjoys wide acceptance today even though the transition between stages can be gradual and difficult to recognize. The developmental process involves the child's increasing motor control followed by increasing problem-solving skills. Ultimately the child achieves symbolic representation through language.

Piaget did not develop a formal instrument to assess a child's progress through these stages, but there has been considerable interest in infant assessment in the United States since the 1930s. The Bayley Scales of Infant Development are the result of years of research and are well regarded among the infant psychometric tests. Sattler (1988) states "they are, at present, by far the best measure of infant development and provide valuable information about patterns of early mental and motor development" (p. 321). In Buros Eighth Mental Measurement Yearbook Damarin describes the Bayley Scales as "an exceptionally well standardized

infant test that grows out of the research traditions of Gesell and Bayley" (1978, p. 293). They are commonly used in medical, educational, and psychological research. Nancy Bayley did not develop these scales based on a Piagetian model, but there has been research on the correspondence between Bayley items and the Piaget stages (Siegel,1981; McCall, Eichorn, & Hogarty, 1977). Sattler (1988) compares the Piagetian and psychometric approaches to assessment and asserts that there are more similarities than differences.

> The significant correlations between Piagetian tests and psychometric tests indicate that children who achieve high scores on psychometric tests of intelligence are not merely 'good test takers'; they have excellent levels of cognitive development in a variety of areas (Sattler, p. 56).

Tests have been developed based strictly on a Piagetian model, but they are not standardized statistically nor do they seek to identify individual differences among children. They do not assume that intelligence is randomly distributed nor that it follows the normal curve. They do not yield a standard score which can be used for comparison of groups or individuals. It is for these reasons that the Bayley Scales were selected over more Piagetian scales to answer the questions regarding the mental, motor, and behavioral status of IVF children relative to their matched peers.

HISTORICAL CONCEPTS

In vitro fertilization is a recent development in the treatment of infertility. The promise of the process took years to become an actuality. In 1959, IVF was successful with rabbits. Steptoe and Edwards began experimenting with human eggs in 1963, and it took fifteen years of work before Louise Brown was born in England (Biggers, 1981). There were some, however, who did not see it as a promising technique but as a foray into dangerous territory, both morally and technologically. Biggers (1981) describes concerns for the ethics of creating and destroying human life, the possibility of genetic engineering, changes in reproductive patterns, and the normality of the offspring. In 1972, Kass cautioned that there was no way of knowing whether the children born of the process would be sterile, deformed, or retarded. Many physicians and others expressed concerns that the parents who seek in vitro fertilization procedures would have undergone many medical manipulations to cure their infertility and that these manipulations might adversely affect the offspring. Some of the concerns expressed by the critics are as follows. The parents would be older in many cases which would put them at risk for chromosomal abnormalities, mostly commonly Down's syndrome in mothers over 40 years of age (Boue, 1988). Fertility is rapidly declining in the normal population by the time many of these couples achieve a first pregnancy which may risk decreased viability of the egg and/or impaired ability of the uterus to support the embryo (Stein, 1985).

The mother's hormonal balance would have been manipulated to produce multiple eggs instead of the usual one per month. The medications used to produce this increase do not necessarily prepare the endometrium for the implantation of the fertilized eggs. The eggs removed from the mother would be exposed to laboratory conditions which could not perfectly simulate natural conditions. The father's sperm would likewise be exposed to laboratory conditions and washed or "prepared" for fertilization. The fertilized eggs would be incubated in a petri dish for a few days before implantation. None of these conditions or methods are known to have mutagenic or teratogenic effects (Biggers, 1981). He goes on to explain that there has been considerable experience with IVF and domestic animals, but he questions whether there has been adequate experience with primates. He anticipates that there may be an increase in cytogenic (genetic aspects of cell structure and function) defects among the embryos but that these embryos would be expected to abort as they do in natural pregnancies. Schlesselman (1979) also refers to the safety of the process based on experience with domestic animals and recommends that a large number of cases will be necessary to determine definitively the risk for humans.

In 1981 Biggers reviewed some of the mechanisms by which defects could occur: the induction of chromosomal aberrations; an increase in the rate of fertilization by abnormal sperm; the induction of point mutations; and the actions of physical and chemical teratogens (agents producing

malformations). Several articles refer to the high rate of embryo loss following implantation as a cause of concern (Schlesselman, 1979; Andrews, 1986). While approximately 25 to 30% of embryos conceived normally are spontaneously aborted (Fishel & Webster, 1987), the rate is much higher for IVF embryos. Angell, Aitken, van Look, Lumsden & Templeton reported in 1983 that the failure rate in IVF implantations is 80%. Angell's research has focused on chromosomal abnormalities, and they report a high rate of chromosomal abnormalities in pre-implantation embryos. They conclude:

> It must be emphasized that over 100 babies have now been born after in vitro fertilization without any apparent chromosome abnormality. Chromosome abnormalities of the kind we have found clearly result in early embryonic loss, and probably contribute to the high failure rate after embryo transfer (Angell, et al., 1983 p. 338).

Another important feature of the IVF process is the increased likelihood of multiple births, which are associated with increased complications at birth and congenital defects (Hendricks, 1966; Andrews et al., 1986; Behrman & Vaughan, 1987). The couple is more likely to achieve a successful pregnancy if multiple eggs are harvested and available for fertilization. The medical centers differ in the decision to implant all fertilized eggs (Tacchi & Dunlop, 1987), but often all viable fertilized eggs are transferred to the mother. Biggers (1981) cites four studies in which this

superovulation in mice and rabbits has resulted in chromosomal aberrations. There is the question as to whether the animal studies in these mammals have implications for a similar risk in humans. Hack, Brish, Serr, Insler, & Lunenfeld (1970) found an increase in congenital anomalies after induced ovulation, but they reported that congenital anomalies were found most often in monozygotic twins, not dizygotic twins. Not all of the eggs implant successfully so that not all result in live births, but twins and triplets are more common than in the general population. The incidence of twins in the general population ranges from one in eighty pregnancies (Groothuis, 1985) to one in eighty-eight for American whites (Behrman and Vaughan, 1987). The rate of triplets to singletons ranges from 1:7,400 (Guttmacker, 1953) to 1:9,000 (Behrman & Vaughan, 1987). This phenomenon of multiple births is associated with increased risks. One such risk is prematurity, and "most twins are born prematurely" (Behrman & Vaughan, 1987, p. 375). Another risk is mental retardation as a complication of prematurity according to Behrman and Vaughan (1987). The American Academy of Pediatrics uses <38 weeks gestational age to denote prematurity (Behrman & Vaughan, 1987), and the more premature the birth the more serious are the risks. Groothuis (1985) states that there is a 15% mortality rate associated with twins (as opposed to 3% with singletons) and that 60% of these deaths are due to prematurity. In addition, there are increased risks for neonatal

complications such as: hypoxia anemia, jaundice, and respiratory distress syndrome. Lancaster (1985) asserts "multiple pregnancies are associated with a higher incidence of congenital malformations" (p. 1162). Behrman and Vaughan (1987) also cite congenital malformations as an etiology for prematurity along with multiple births. Multiple births are associated with lower birth weights and complications at delivery. Lancaster (1985) cites the increased rate of Caesarean section deliveries among these births as a possible reflection of "obstetric complications and more frequent intervention in high risk pregnancies" (p. 1160). Finally, Groothuis (1985) asserts that there is general agreement in the medical literature that twins are delayed in the acquisition of verbal and motor skills in the first year but generally have overcome this delay by four to six years of age. In 1965, Hirsch, Langford, and Jansky reported at the annual convention of The American Orthopsychiatric Association a follow-up of 54 premature children. They were compared to 53 mature children. The children were administered 36 tests covering broad developmental aspects at kindergarten and were tested again in first and second grades for academic skills. The premature children did uniformly poorly on all measures but especially on language and scholastic tasks. These authors suggested that the premature children demonstrate "more primitive central nervous system patterning" (p. 358) and that this was important because 4% of the school population was premature. While this study is

over 20 years old, it was cited by Schenker, Yarkoni, and Granat in 1981 as evidence of a long-term risk for the prematurely born as a result of multiple pregnancies.

In addition to these factors which are commonly cited in articles about IVF, there are some less often cited concerns. Hubble, an attorney writing in 1981 about the physician's legal liability in this process, cites "an estimated 3% additional risk of abnormality in IVF offspring suggested by animal studies" (p. 505). There is concern about polyspermy wherein the eggs can be simultaneously fertilized by two sperm instead of one since the quantity of sperm reaching the eggs may break down their ability to block entry of additional sperm. There is concern whether defective sperm which usually do not reach the eggs under normal circumstances will have an equal opportunity in the petri dish and therby increase the risk for abnormalities (Englert et al., 1987; Kruger, et al., 1988; Lian et al., 1986). Hubble (1981) also looks ahead to future generations and speculates that some defects may not manifest themselves in the IVF child but may do so in that child's offspring if the defect should be recessive.

It is presumed by Angell and others that embryos conceived by this method will be subject to the same laws of nature which result in spontaneous abortions when there are major genetic defects or a hostile environment. Less life threatening defects may, however, be more common, and it is unknown whether any of these would compromise the cognitive

skills of the child. Hunt's review of the literature indicates that there is a growing body of evidence

> ...delineating relationships between perinatal environmental insults and measured infant intelligence. There is evidence that infant development may be a more sensitive indicator of some perinatal events than is later development, perhaps because of the larger effects of environment beyond infancy on measures of childhood intelligence" (1976, p. 252).

In 1970 Nancy Bayley, the originator of the scales used, wrote:

> ...mental abilities as measured by standard tests are a function of (or the end product of) many determinants. These determinants include, first, the human organism with its basic complements of neurons, sense-perceptors, motor reactors, hormones, enzymes along with their organizing tendencies for action and reaction to the environment. There is much still unknown about the determinants of individual differences among these...There is also the possibility of various kinds of prenatal and paranatal 'environments' resulting in damage or interfering with the development of optimal function (p. 1164).

In short, the biological integrity of the child is an important aspect in the cognitive and behavioral development of that child. The medical manipulation of the mother's body and the exposure to laboratory conditions of both the eggs

and sperm may compromise these children in a subtle manner so as to interfere with the "development of optimal function".

PREVIOUS RESEARCH

The first child born through IVF arrived in 1978 in England. In 1983, Hilson, Steptoe, Edwards, and Purdy wrote a letter to the editor of Developmental Medicine and Child Neurology regarding their follow-up on the first two IVF infants in England. It should be noted that Steptoe and Edwards were the pioneers in the world's first successful IVF births. The two infants were fourteen and twenty months of age. The assessment was multi-faceted and included psychometric evaluation on the Griffiths Mental Development Index. Both children had normal psychometric results on all five scales of the Griffiths. The physical findings were normal as well except that the second child had congenital ptosis (drooping eyelids).

There was no follow-up study as to the well-being of other IVF children until 1985 when a survey was done in Australia and New Zealand. This survey was conducted by the National Perinatal Statistics Unit of the Fertility Society of Australia. It covers the years 1979 to 1984. All 660 IVF infants were included; likewise,all pregnancies which went to at least twenty weeks gestation were included. It also included six stillbirths. The parameters reported included the mother's age, plurality/outcome, infant's sex, gestational age, birth weight, and congenital malformations.

The techniques were a physical examination and chromosomal studies where indicated. These findings were compared with the national statistics on major congenital malformations for single and multiple births. Sixteen children were found to have major congenital malformations which followed no discernible pattern. These included heart disease, spina bifida, and trisomy 18 (associated with 90% mortality in the first year, severe mental deficiency, and a wide variety of dysmorphic features [Smith, p. 10-11]). There was no statistical analysis done; the results were reported simply as percentages. The conclusions were that IVF carries only a minimal increase in risk for congenital defects, but more investigation into the heart defects was recommended. This study made no attempt to assess the cognitive, motor, or behavioral characteristics of the children.

Also in 1985, 244 Australian IVF pregnancies were analyzed by Lancaster who obtained information from eight IVF centers. He commented on the early stage of IVF as a treatment, the small numbers of children available for study, and the lack of follow-up except as summary figures. He developed a register of these children "to discover whether the incidence of congenital malformations was increased" (p. 1160), and other pregnancy outcomes were reported also. The time frame for this sample was 1979 to 1983. He reports that of 244 pregnancies, only 135 resulted in live births. The rates of biochemical pregnancies, ectopic pregnancies, and spontaneous abortions were all higher than published figures

for natural pregnancies. Spontaneous abortions increased with maternal age, a typical finding in natural pregnancies. While the Australian national average for multiple births is 1%, the rate for this sample was 22%. Twins accounted for 19% and triplets for 3%. As a result of the large number of multiple pregnancies, 23% of the births were premature. Of the singletons their prematurity rate was three times the national average. Birth weight was also lower due to the high number of multiple births. The number of girls and boys was almost equal. Major congenital malformations, however, were below the national average of 1.5% to 2.0%; the rate for IVF babies was only 1.1%. There were two malformations reported; one involved a heart defect, and the other involved a congenital dislocation of the hip. There was no systematic study of chromosomal abnormalities.

Lancaster (1985) cites the problem of identifying an appropriate control group since without IVF these couples would probably not have conceived a child. Comparison with "the general obstetric population is not ideal, but it does at least put the overall results of in vitro fertilisation in perspective, even if the reasons for various outcomes of pregnancy cannot readily be determined" (p. 1162). There was no attempt to assess the children cognitively or behaviorally He concludes:

> There are several possible reasons why an increased incidence of chromosomal abnormalities or structural congenital malformations might occur after in vitro

> fertilisation....Against this background it is reassuring that the incidence of such abnormalities and malformations was no higher after in vitro fertilisation than in other pregnancies, but numbers were small and ... cytogenetic studies were not routinely performed on abortuses or other products of coneption (1985, p. 1162).

He supports further research on larger numbers because there were expected and unexpected findings.

Lancaster published again in Lancet in 1987 on the subject of congenital malformations in the IVF population. The data covered the years 1979-86 and included 1694 live births. This time a congenital malformation rate of 2.2% was reported. Six children had spina bifida, some with other malformations. Four children had transposition on the great vessels, a heart defect. He believes that there is a low probability that these are "chance findings" (p. 1392). Although these figures are higher than in the previous report, the rate of malformations is still consistent with the Australian national average. He believes that these numbers are still insufficient to be certain, and he is impressed by the tendency for spina bifida and heart defects to be disproportionately represented.

Another follow-up study was published in 1985 by Mushin based on the Australian experience, and this study assessed psycho-social issues as well as physical well-being. Mushin believed it worthwhile to look at the parenting capacity of

the couples suffering through years of infertility, the vulnerability of these children to be seen as "special" with accompanying unreal concerns or expectations, the marital relationship, and the physical condition of the child. Forty-nine of the fifty-two children born through the Monash University program were included; one child had died at 4.5 months of age, and the parents of twins refused to participate. The procedures were a pediatric evaluation, psycho-social interview of the parents, administration of the Bayley Scales of Infant Development, and observation of the family functioning and interacting in the interview setting. Mushin states, "The Bayley Scales ... were chosen because they are well-researched and standardized and commonly used for developmental evaluation of children in the age range seen" (1985, p. 871). The principal findings are as follows:

1. The incidence of caesarean section is more than twice the normal rate. Prematurity was four times the normal rate, very low birth weight was ten times the normal rate, and twin births occurred twenty times the norms.

2. Four families were found to have significant clinical issues. In three of these the problems involve significant physical problems.

3. Less severe clinical features included colic, asthma, and neonatal jaundice.

4. On the Bayley Scales 85% demonstrated normal mental, motor, and social skills and abilities. The children falling below the average range were those with physical

abnormalities. These findings were felt to be reasonable in light of the physical problems of low birth weight and multiple births.

5. Psycho-social problems were relatively infrequent and considered to be of mild degree.

The authors conclude that the IVF process has an acceptable rate of risk for physical defects, and the "degree of interactional problems found is not considered abnormal" (1985, p. 873).

Mushin published again in 1986 using some of the same data. This publication includes only thirty-three of the original forty-nine children; there is no explanation as to why some were omitted. Because this study uses the same data, the same conclusions are drawn. There is more information as to gestation and method of delivery, problems related to infertility, and the number of IVF cycles. The Bayley results are reported only for those children found to have major or minor problems. He concludes,

> There were no instances of severe psychopathology such as child abuse or neglect, nor were there children with developmental delay which was not explained by physical problems. The range of results from developmental assessment is considered acceptable for a population of 1 to 3 year olds (1986, p. 251).

He does not report whether the children's ages were corrected for prematurity nor are there any group results reported. He cites a need for a control group in order to interpret these

results with more confidence. This study has been reported in three different journals: Australian Pediatric Journal, Journal of In Vitro Fertilization, and Clinics in Obstetrics and Gynecology.

In 1986, Yovich, Parry, French, & Grauaug published another follow-up study based on Australian IVF children. In this study the first twenty infants to reach their first birthday were evaluated as to history, physical condition, and mental status. This time the Griffiths Developmental Scales were used; these are the British equivalent of the Bayley Scales. Physically there was only one infant with a significant abnormality and two more with minor abnormalities, one of which required surgical correction. As before, there was an increased rate of multiple pregnancies, caesarian deliveries, and low birth weight babies. This is the first study which reports the developmental findings in detail. The average chronological age at evaluation was 12.53 months while the mean mental age was 14.72 months. Only one child had a general quotient (GQ) below 100, and this was a child with low birth weight. The author also discusses correcting the chronological age to adjust for prematurity. The mean general quotient was 117.48 when this adjustment was made. The parents were reported to have a low anxiety level despite the media attention they had received. The problems of preterm births and low birth weights generally coincide with multiple births but may relate to the mother's infertility history. He goes on to say:

> It is reassuring to note that the developmental assessment for five test scales was in advance of the mean rates defined by Griffiths. However, it cannot be concluded that these infants have advanced development, as a control series was not defined or studied. Nevertheless, the concept of a general development quotient (GQ) has been standardized and continues to work surprisingly well in clinical practice (1986, p. 256).

This study includes the most detail regarding the psychological measures. The mean and standard deviations of the Griffiths are not reported, but one assumes that the mean is 100. Again the need for a control group is stated.

It is interesting that all of these studies have originated in New Zealand or Australia. There have been no American or British studies published to date. None of these studies has a control group, much less a matched control group. This study is the first in this hemisphere to evaluate the IVF children, and the first in the world to have a control group. The studies so far are encouraging that these children are at least average and that the risk for abnormality is acceptable. All studies cite the increased frequency of multiple births as a major risk factor which may impact upon developmental status and which needs to be addressed.

In 1985, Hejtmancik, Ledbetter, Beaudet, & Quigley reported the first case of a chromosomal abnormality in the

IVF population in the United States and after 600 live births worldwide. It involved Trisomy 21, and the child was born to a 28 year old mother. The genetic analysis found that the nondisjunction was present in the father which suggested that the IVF process was non-contributory in this case. He speculates that a sperm with this defect might not have reached an egg in the Fallopian tubes, but it had equal access in the petri dish. He recommends amniocentesis when there are "routine indications such as maternal age" (1985, p. 831).

Steele and Wenger in 1987 reported a case of Trisomy 18 in a full-term female. She demonstrated multiple congenital abnormalities associated with this defect. Both parents had normal children by previous marriages. Based on 1500 live IVF births, they calculate that the risk of a chromosomal aberration is approximately 1/160 or approximately 1/700 for the autosomal trisomies. They report that this is similar to that of in vivo births and that monitoring protocols can be the same as for in vivo pregnancies.

In 1986, Andrews et al. published a follow-up study of 125 IVF pregnancies from The Jones Institute in Norfolk, Virginia. The 125 pregnancies resulted in 100 deliveries with 115 babies. This coincides very closely with the sample used for this study. Three children died due to prematurity, but "no congenital abnormalities were found" (1986, p. 849). In the first trimester 26 multiple pregnancies were determined by ultrasound, but the multiple delivery rate was

only 14%. The average number of eggs implanted was 3.2. There were three children identified as having congenital abnormalities. One had a neural tube defect, one had a heart defect which required no treatment and a kidney defect which was surgically repaired. One was born with much of the external ear missing but hearing was reportedly normal. These authors refer to the research being undertaken by the NICHHD grant; at that time 21 children had been "intensively evaluated" (1986, p. 851.). Nine abortuses were examined, and two demonstrated chromosomal defects. The only positive findings involved the high number of multiple pregnancies, and a high rate of vaginal bleeding during the pregnancy. They acknowledge the risks of multiple births (prematurity, fetal loss, and abnormality) but assert that the "incidence of prematurity ...appears comparable to that of general experience when multiple pregnancy and intrauterine abnormalities are considered" (1986, p. 851). They claim that their investigation for congenital abnormalities was

> intense and probably accurate. The three babies having major abnormalities among the 115 babies described here are consistent with results in studies of larger groups reporting incidences from 2.1% to 3.3% but final conclusions must await larger numbers. The increased proportion of multiple pregnancies will predispose to a higher proportion of major abnormalities among babies conceived in vitro (1986, p. 852).

They also reported a cesarean section rate of 56% which they believe represents increased multiple births, older maternal ages, and an increase rate of hypertension.

In 1986, a national registry was established in the United States by Medical Research International and The American Fertility Society Special Interest Group to collect information regarding IVF, frozen embryo transfers, and gamete intrafallopian transfer (GIFT). Data collection began in 1987, and its purpose is to provide descriptive information rather than to test hypotheses or to analyze results statistically. Participation is voluntary, and the registry does not include the data from all IVF centers. Their first publication tracks chromosomal abnormalities and congenital abnormalities by year. In 1985 one chromosomal abnormality and two congenital anomalies were reported. In 1986 there were three chromosomal abnormalities and nine congenital abnormalities. They are not classified as major or minor, and this author detected no trends in the defects reported. This is a higher number than available elsewhere in the literature search. The Registry plans to do statistical analyses in the future and longtitudinal data analysis. Marrs, past president of the IVF Special Interest Group of The American Fertility Society, comments at the end of the report:

> The information contained within is critical for the medical community to scrutinize and helpful for the lay public to better understand the problem of less

> than optimal outcome persisting within these technologies (1988, p. 215).

SUMMARY

It has been nearly thirty years since IVF was proven successful with a domestic animal, and it has been ten years since the first human offspring. Much concern has been expressed by physicians, scientists, and the public over the well-being of the offspring which now number in the thousands. Many authors speculated on how IVF would differ from in vivo conception. Some studies have followed up on the pregnancies, and some others have followed the children. Some are reassuring that the risk is minimal and acceptable. Others are less optimistic. To date, however, there has been no controlled study with large numbers of children to address these concerns. This research has addressed the psychological outcomes for the IVF offspring and matched controls and has correlated the findings with identified risk factors such as multiple births/prematurity and maternal age. While the numbers in this study are not large enough nor the children old enough to resolve all issues, this study is a major milestone in the follow-up of this new population.

CHAPTER 3

This research was undertaken under a grant from the National Institute of Child Health and Human Development (NICHHD). The grant was carried out by The Eastern Virginia Medical School and The Children's Hospital of The King's Daughters in Norfolk, Virginia. The methodology was jointly agreed upon by the NICHHD and the participants in Norfolk. The data was collected between January 1985 and March 1987.

SAMPLE

Cases

The IVF babies have all been conceived at The Howard and Georgeanna Jones Institute of Reproductive Medicine in Norfolk, Virginia. They had birthdates between October, 1983, and September, 1985, and there were 110 eligible children. Although the children were all conceived at one location, the parents represented a geographically diverse group including some from foreign countries. All of the family's expenses associated with participation in this follow-up grant were paid under terms of the grant.

CONTROLS

The cases were matched from the civilian obstetrical population within one hundred miles of Norfolk. The cases were geographically so diverse that it was not feasible to obtain the controls from their geographical locations. Not only was it economically infeasible, but it was believed that cooperation would be difficult to obtain from the families selected as the matches.

The cases were matched based on age of the infant (± 3 months), maternal age (± 3 years), number of births per pregnancy, sex, and race. Parental education and income were matched when possible. The matching was done by an epidemiologist using hospital records; fifteen hospitals within the specified radius around Norfolk participated. When a potential match had been identified the attending physician was contacted and asked whether there were any contraindications to contacting the patient. The selected family was then contacted by a letter explaining the study and their role.

PROCEDURES

Data Gathering Methods

The psychological evaluation was one of five procedures undertaken on each child thirty months of age or younger. The other procedures were a general physical examination, a neurological evaluation, a cardiac examination, and an ultrasound examination of internal organs. These

examinations were conducted to identify any major or minor malformations or congenital abnormalities. A widely accepted definition of major and minor malformations was used to describe any positive findings; those malformations which generally cause functional impairment or require surgical correction were defined as major, the remainder as minor (Holmes, 1976). Except for a small number of the cardiac examinations, all examinations were conducted by the same examiner in each specialty.

The epidemiologist obtained a pregnancy history based on a maternal interview to identify other possible sources of congenital malformations such as: medications, infections, alcohol/drug abuse, genetic factors including previous malformed infants, and environmental and occupational exposures. Data regarding parental education and family income were also collected in this interview.

The physicians and psychologist performing the evaluations were blind as to the status of the child, whether case or control. Parents were advised not to reveal any information which would inform the examiners as to the child's status. All examinations were performed in the same location within The Children's Hospital of The King's Daughters.

The psychological evaluation consisted of administration of The Bayley Mental and Motor Scales and was done as the first procedure of the day whenever possible to obtain the best cooperation. All were administered by the

same examiner. A parent was present with the child to minimize any separation anxiety and to assist in administration if necessary.

If the child was premature, the age was corrected for the amount of prematurity; all scores are based on the corrected age where applicable. This is a widely used procedure to correct for the degree of prematurity (Caputo, Goldstein, & Taub, 1981; Hunt, 1976), but there is some controversy over its use. Siegel (1983) indicates that the corrected and uncorrected ages have equal predictive power after twelve months of age. There has been a precedent for this procedure in the Yovich et al. study discussed in Chapter 2.

The findings were reported to the parents in age equivalents; this is a readily understandable concept and avoids the problem of the Mental or Psychomotor Development Index being interpreted as an early indicator of child's later intellectual quotient by the parents. The Behavior Rating Scale was completed by the school psychologist at the end of the session, but no behavioral report was made to the parents.

Ethical Safeguards and Considerations

The families of both cases and controls were fully informed as to the nature of the study by letter when invited to participate. They were advised again verbally

upon arriving for the session. A consent letter was signed by each family which detailed the procedures and informed them that none of the procedures carried any risk based upon current medical knowledge (Appendix B). All were informed of their right to withdraw at any point and of the intention to publish the results. Each family was guaranteed of their anonymity and how to obtain the results of the study.

INSTRUMENTATION

Description

The Bayley Scales of Infant Development were published in 1969. They are the results of infant testing begun in 1933 by Nancy Bayley when she published the California First Year Mental Scale. As Damarin states in his Buros review of the Bayley, "Most of the items ... have seen extensive service in longtitudinal research. Many of them have been revised, used in large-scale research projects, re-revised, tried again, and revised once more" (1978, p. 206). Bayley designed the scales to

> assess sensory-perceptual acuities, discriminations, and the ability to respond to these; the early acquisition of 'object constancy,' memory, learning, and problem solving ability; vocalizations and the beginnings of verbal communication, and early evidence of the ability to form generalizations and

> classification which is the basis of abstract thinking (1969, p. 3).

This is her description of the content of the mental scale. The Mental Scale consists of 163 items arranged in order of difficulty as determined by her research. They are a mixture of verbal and non-verbal items. The materials are very similar to those in most of the infant scales: blocks, pictures, noise makers (e.g. a bell, rattle), formboards, and toys. The same materials are used at a various levels of complexity. The child's performance is expressed as a Mental Development Index (MDI) with a mean of 100 and a standard deviation of 16. Another way to report the child's performance is in terms of an age equivalent. That is determined by locating the age in the norms where the child's raw score is closest to 100. There is a minimum value of 50 and a maximum of 150.

The Motor Scale consists of 81 items of increasing complexity. The motor scale is designed to be "a measure of the degree of control of the body, coordination of the large muscles and finer manipulatory skills of the hands and fingers" (Bayley, 1969, p. 3). These tasks are not considered to be cognitive in nature, and there is little correlation between a child's performance on the two scales. The child's performance is expressed as a Psychomotor Development Index (PDI) with the same mean and standard deviation as the MDI. The results of the Motor Scale can

also be reported as age equivalents using the same procedure as for the Mental Scale described above.

The Bayley Scales are often described as the best standardized of the infant psychometric tests available because the norming procedure involved 1262 infants of all ages and represented the U. S. population demographically. Damarin states, "The standardization of the mental and motor scales is as good as or better than that of any other individual test, whether for infants, children, or adults" (1978, p. 292). The norms for the newborn are presented in half-month intervals; beginning at six months, the norms are in monthly intervals.

The reliability data in the manual is based on a split-half analysis. The author was careful to group all items in a series onto only one half to avoid spuriously high correlation coefficients. The Mental and Motor Scales were both evaluated in this way. The correlation coefficients for the Mental Scales range from .81 to .93 with a median value of .88. The values are lower for the Motor Scale (.68 to .92) which she attributes to the smaller number of total items. The median value for the Motor Scale is .84.

The test-retest reliability was found to be 76.4% for the Mental Scale and 75.3% for the Motor Scale. It should be noted, however, that only 28 cases were involved in this study. Damarin (1978) criticizes this reliability research for two reasons. This research is based on precursors of the Bayley Scales and reports percentages of agreement; he

would have preferred product-moment correlations. The test-retest interval was also too short in his opinion. This may have resulted in "too optimistic an impression of the reliability of the scale over longer periods of time" (1978, p. 292).

Another measure of reliability is the standard error of measurement. The range of standard errors of measurement for the Mental Scale is 4.2 to 6.9 standard score points. For the Motor Scale it is 4.6 to 9.0.

The validity of the Bayley Scales is not addressed in the manual for children under the age of 24 months. Predictive validity is inappropriate since much research has demonstrated conclusively that infant tests do not predict later IQ (Honzik, 1976; McCall, 1979). Damarin discusses the evidence "that the abilities measured by the Bayley mental scale may change qualitatively with age" (1978, p. 292). The result is that infant scales "may fail (in normal populations) to predict themselves" (Damarin, 1978, p. 292). There has been some concurrent validity research done on children 24 months and older. The manual states that the correlation with the Stanford-Binet (Form L-M) is .57 based on a sample of 120 children.

The Infant Behavior Record (IBR) consists of thirty decriptors to address the child's affect and behavior during the evaluation. Twenty of them are constructed on a nine point rating scale with verbal descriptions for each point. These twenty include such categories as: social orientation,

cooperativeness, fearfulness, activity, reactivity, and sensory areas of interest. There is no consistent pattern as to the value of a point on a scale; a rating of five may be a desirable or undesirable behavior depending on the category. There are also additional clarifying descriptors for some of the categories, but there are no numerical values for these. There are six more categories on five point scales. Again, there is no consistency as to the value of a number; each must be examined individually. There are four more items which use only a two point scale. A child's behavior can be recorded in great detail using the Behavior Record, but it yields no score. In the test manual there are tables providing the modal value for each category at different ages, but there is no standardization of these behavioral descriptors beyond that. Matheny (1983) reports that these behaviors are not stable during the ages of six to twenty-four months. Damarin (1978) in his review of the Bayley does not mention the Behavioral Record. Wolf and Lozoff (1985) discuss the construction of the Behavior Record and the problems it presents for analysis. They state:

> Poorly adaptive behavior may be reflected by ratings that are high, low, or both, depending on the item, and because no assumptions can be made about the distribution, whether normal or any other, of these qualitatively ordered scales, appropriate statistical techniques are uncertain...Perhaps because of these

> problems, the only published analytic standards consist of modal ratings for every 2 to 3 months of infant age, and the IBR is frequently omitted when the BSID is administered (p. 200).

While behavioral factors during an evaluation may affect the child's performance and the score, there has been limited use of behavioral observations. Wolf and Lozoff go on to say:

> Yet clinicians and researchers often need to compare the behavior of groups of babies, to analyze the behavior of infants who vary in age, to assess behavioral change following an intervention, to relate behavior to other factors such as developmental test performance, to identify unusual or deviant behavior, or simply to characterize the behavior of an individual infant (1985, p. 200).

This IVF research will be comparing the behavior of cases and controls and will be looking for unusual or deviant behavior in either group. This data is difficult, however, to analyze because the questionnaire is inconsistently numbered and because there is a paucity of research on its interpretation.

RESEARCH DESIGN

This is an epidemiological study to determine the association between congenital malformations (birth defects), mental/motor/behavioral differences and exposures and/or outcomes. According to Mortensen, Sever, & Oakley (1986) this involves three major issues. The first is the "definition and ascertainment of outcomes of interest". The second is the "definition, identification, and quantification of exposures or of other risk factors". The third is the "use of epidemiological and statistical techniques to determine the strength of the association" (1986, p. 189). Usually it is difficult to identify the exposure, but in the case of IVF the exposure is defined as the IVF process itself along with any other environmental or genetic factors which are also recognized and can be ascertained.

This research was conducted using descriptive methodology, one of the primary methods of epidemiological research (Mortensen et al., 1986). This type of study yields information about the rates of occurrence, the populations at risk, and the time and/or place of risk. This requires that the cases be clearly defined and identified. In the case of IVF children this can be done with great certainty.

This research is based on both self-report and observations. The epidemiologist interviewed the parents on a lengthy questionnaire as to the parents' health, the

pregnancy, exposure to recognized teratogens, labor, delivery, and socioeconomic status. The observations involved the examinations of all the professionals. The physicians designed observational report forms for their specialties, and the school psychologist used the copyrighted Bayley Scales of Infant Development.

The purpose was to collect data to assess the current status of the IVF population of children. There was no treatment or intervention.

NULL HYPOTHESES

It is anticipated that there will be no difference between the IVF infants and their matched controls on the Mental Development Index, Psychomotor Development Index, or on the behavioral indicators.

A confidence level of p=.01 was established as the measure of statistical significance. These children were evaluated in such detail that a strict confidence level can be justified to minimize the risk of a Type 2 error.

STATISTICAL ANALYSIS

T-tests were conducted to compare the Mental and Psychomotor Development Indexes of the two groups. T-tests were also used to evaluate the matching on infant's age and maternal age.

Chi-squares were done to correlate the birth weight and gestational age with the Mental and Psychomotor Development Indexes to determine whether these risk factors associated with prematurity resulted in lower values in IVF children.

Spearman and Pearson correlation coefficients were conducted to determine whether there were any correlations among the Mental and Psychomotor Development Indexes and the gestational age, maternal age, and parent education.

SUMMARY

The research questions addressing the normality of children conceived through in vitro fertilization required a descriptive research methodology. The IVF children born in one United States center were matched and then evaluated by a multi-disciplinary team in Norfolk, Virginia. The physical examinations looked for congenital abnormalities (birth defects), and the psychological evaluation looked for cognitive, motor, and behavioral differences. Statistical analyses focused on similarities between the cases and controls and correlations between the findings and previously reported risk factors.

CHAPTER 4

COMPLIANCE

Of the 110 children conceived through IVF at The Jones Institute between October 1983 and September 1985 only 83 actually participated in the study. Two cases could not be located, and three foreign cases were not contacted due to the costliness of their participation. Eight families refused to participate including two sets of twins and one set of triplets. Seven of these refusals were due to conflicting obligations, and one was due to the protective nature of the parents. None indicated that the refusal was due to the physical condition of the child. This brought the total number of non-participants to seventeen. Ten more did not participate who had originally agreed to participate due to scheduling, transportation, or other logistical problems near the end of the study. This brought the final case sample to 83.

The controls were identified simultaneously. Of the 105 selected, 98 of the first choices agreed to participate. Five second choices and two third choices also agreed. One refused for religious reasons. One refused because the child had developed an adverse reaction to an immunization. Five refused for conflicting family obligations. Again,

none cited the physical condition of the child as the reason for refusing.

As it became apparent that the case would not be participating, the match was excluded. This reduced the control group to 93. There were ten instances where the IVF child could not be evaluated for logistical reasons at the end of data collection, but their matches were included in the analysis because they had already undergone their evaluation.

The total study included 176 infants (83 cases and 93 controls), but only 129 were evaluated using the Bayley Scales because their ages were within the norms of 30 months. A serious effort was made to get all children in for the evaluations before they passed 30 months of age, but this was impossible in some cases. Two children refused to cooperate enough during the Bayley administration to obtain valid psychometric results, and no MDI or PDI scores are available for them. The behavior rating scales were, however, completed for these children. The control with Trisomy 13 was too physically handicapped to be evaluated on the Bayley, and no scores or behavioral ratings were recorded for her. The children over 30 months of age underwent the other four evaluations but were not assessed by the school psychologist.

MATCHING VARIABLES

Maternal Age

The cases were matched based on maternal age (±3 years). The statistical analysis (Appendix C) indicates that the mean maternal age for IVF children was 34.5 years with a standard deviation of 3.6 years. The range was from 27 years to 43 years. For the controls the mean maternal age was 33.2 years with a standard deviation of 3.6 years. The range was from 25 to 41 years.

This finding is consistent with a trend since 1976 that maternal age is increasing (Wegman, 1987). Although most births are to women between 15 and 24 years, in 1986 25% of births were to women 30 years and older (Wegman, 1987).

Child's Age

The ages of the infants were matched ±3 months. The IVF children's mean age was 17.3 months with a standard deviation of 6.4 months (Appendix D). The range was from 10 to 29 months. The mean for the controls was 15.8 months with a standard deviation of 4.1 months. The range was from 9 to 29 months. The difference in means of 1.5 months was nonsignificant ($p=.13$).

Race/Gender

The children were likewise matched based on gender and race. Among the IVF cases 55.4% were male. Among the

controls 55.9% were males. There was one black IVF male and one black control.

Births per Pregnancy

The children were matched based on the number of births per pregnancy. Twins could be matched within the one hundred mile radius used for singletons, but it was necessary to go beyond that radius to match triplets. This was done by consulting an organization known as The Triplet Connection. There were 11 sets of twins in the IVF group and 10 sets in the control group. There were two sets of triplets in the IVF group and three sets in the control group.

Twins occur in one of 80 to 86 pregnancies among American whites according to different authors (Groothuis, 1985; Behrman & Vaughan, 1987). With a total original sample of 110 IVF children, two sets of twins might be expected. Of the original 110 there were 11 sets of twins. Triplets occur in one of 7400 to 9100 pregnancies according to different authors (Guttmacher, 1953; Behrman & Vaughan, 1987). With a group of only 110 a triplet pregnancy would be unlikely, but there were three. This population is different from the general population in terms of the frequency of multiple births.

Socioeconomic Status

The socioeconomic status of the family was matched, but this was the lowest ranking of the matching variables. The mean parental education was determined and placed on a 9-point scale ranging from less than a high school diploma through graduate degree. The results are presented in Table 1. There were nine instances where this information was unavailable. No participants had less than a high school education so the first two points on the 9-point scale were empty, and ninety-three had at least a bachelor's degree. Of those having at least a bachelor's degree, 60.2% were in the control group. The control parent group was significantly better educated than the IVF parent group ([6, N=130] = 17.063, p=.009). The Mantel-Haenszel chi-square was also calculated; (1, N=130) = 2.089, p=.148, which would not be significant. Because some cells have fewer than five in the count, the chi-square value may not be valid.

According to the U.S. Bureau of the Census, in 1986 (the year when much of the study's data was collected) 20.1% of the white population had a bachelor's degree or more (p. 125). In the IVF group the percentage is 63.7, and in the control group the percentage is 77.7. Neither group is representative of the U.S. population in terms of education.

Income was also requested but was unavailable in seventeen instances. It was divided into a 6-point scale ranging from $10,000 to $65,000+ per year. These results

Table 1

Chi-square Comparison of IVF Cases and Controls on Parent Education

FREQUENCY PERCENT ROW PCT COL PCT	CASE	CONTROL	TOTAL
H.S. GRAD	3 2.31 100.00 5.17	0 0.00 0.00 0.00	3 2.31
TECH SCHL	0 0.00 0.00 0.00	4 3.08 100.00 5.56	4 3.08
SOME UNIV	11 8.46 84.62 18.97	2 1.54 15.38 2.78	13 10.00
2 YR UNIV	7 5.38 41.18 12.07	10 7.69 58.82 13.89	17 13.08
4 YR UNIV	16 12.31 35.56 27.59	29 22.31 64.44 40.28	45 34.62
B.S.+	18 13.85 42.86 31.03	24 18.46 57.14 33.33	42 32.31
GRAD DEG	3 2.31 50.00 5.17	3 2.31 50.00 4.17	6 4.62
TOTAL	58 44.62	72 55.38	130 100.00

FREQUENCY MISSING = 9

STATISTICS FOR TABLE OF MEAN_ED BY CASECNTL

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	6	17.061	0.009
LIKELIHOOD RATIO CHI-SQUARE	6	20.255	0.002
MANTEL-HAENSZEL CHI-SQUARE	1	2.089	0.148
PHI		0.362	
CONTINGENCY COEFFICIENT		0.341	
CRAMER'S V		0.362	

are presented in Table 2. There was a non-significant difference; χ^2 (5, N=122) = 8.188, p=.146. While the IVF procedure is very expensive, these groups are not significantly different in terms of family income.

According to the U.S. Census Bureau, in 1986 35.2% of the white households had annual incomes of $35,000 or more (p. 422). In the IVF group 87.0% had incomes of $35,000 or more, and 79.4% of the control group did. Again, neither group is representative of the U.S. population. Both groups are affluent, and the IVF group is more affluent than the control group with 42.6% having incomes of $65,000 or more compared with 26.5% of the control group.

PHYSICAL FINDINGS

The final report of the study by Morin et al. (1988) indicates that only six major congenital malformations were detected, but they involved only three children: two cases (2.4%) and one control (1.1%). This difference was reported as nonsignificant in the team's final but as yet unpublished report (Morin, et al.). This author has no direct access to the statistical analysis. There were no alternate explanations found that would account for the major malformations. None of the mothers had prior malformed infants or history of fevers, infections, alcohol or drug use during pregnancy.

Table 2

Chi-square Comparison of IVF Cases and Controls on Family Income

INCOME	CASECNTL		
FREQUENCY PERCENT ROW PCT COL PCT	CASE	CONTROL	TOTAL
$10,000-19,999	2 1.64 66.67 3.70	1 0.82 33.33 1.47	3 2.46
$20,000-34,999	5 4.10 27.78 9.26	13 10.66 72.22 19.12	18 14.75
$35,000-44,999	10 8.20 30.30 18.52	23 18.85 69.70 33.82	33 27.05
$45,000-54,999	8 6.56 53.33 14.81	7 5.74 46.67 10.29	15 12.30
$55,000-64,999	6 4.92 50.00 11.11	6 4.92 50.00 8.82	12 9.84
$65,000+	23 18.85 56.10 42.59	18 14.75 43.90 26.47	41 33.61
TOTAL	54 44.26	68 55.74	122 100.00

FREQUENCY MISSING = 17

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	5	8.188	0.146
LIKELIHOOD RATIO CHI-SQUARE	5	8.353	0.138
MANTEL-HAENSZEL CHI-SQUARE	1	4.703	0.030
PHI		0.259	
CONTINGENCY COEFFICIENT		0.251	
CRAMER'S V		0.259	

One case had a non-patent auditory canal, partial hearing loss in one ear, and microtia (small ear). These findings were reported in the review by Andrews et al. (1986); it was reported there that this child's hearing was normal, but this evaluation indicated a loss. Another case had a thoracic myelomeningocele which resulted in motor deficits on the Bayley Psychomotor Scale; his MDI was 50, or three standard deviations below average. The major malformation in the control group was a genetic Trisomy 13 with microcephaly, hearing loss, and coloboma of the iris resulting in severe loss of vision. These are classic features of this syndrome along with severe mental retardation (Smith, 1976). This child was unable to be assessed on the Bayley Scales due to her physical handicaps. While it would have been desirable to include an MDI value for this child in the statistical analysis, any value chosen would have been no more than a guess and difficult to defend.

A variety of minor malformations were found in both populations. Two approached statistical significance, but not clinical significance. A minor malformation in the helix of the ear known as a Darwinian tubercle was found in five cases but no controls ($p=.019$). This is an autosomal dominant feature with a high incidence in European families; it is seen in 20% of German births and in 55% of English births (Bergsma, 1979). "It requires no treatment and has no impact on life span or function" (Bergsma, 1979, p. 288).

High arched palates were found in nine cases and two controls (p=.025). Five of the nine cases with high arched palates were low birth weight infants (less than 2500 grams).

Neurological abnormalities were limited to controls. These included the case of Trisomy 13 and two others. None of the differences were significant statistically according to the final report (Morin, et al., 1988, unpublished).

In regard to the other physical examinations, there were no significant differences between the two groups on the abdominal ultrasound, cranial ultrasound, or the cardiac examination.

PSYCHOLOGICAL RESULTS

Mental and Psychomotor Development Indexes

T-tests were done on the two groups to compare the Mental Development and Psychomotor Development Indexes. The results are summarized in Tables 3 and 4; see Appendix D for more detail.

Table 3

T-test Results on Mental Development Index

Group	N	Mean	Min.	Max.	DF	T	Prob.
IVF	63	114.97	92	140	127	1.56	.12
Control	66	111.38	78	141	127	1.56	.12

Table 4

T-test Results on Psychomotor Development Index

Group	N	Mean	Min.	Max.	DF	T	Prob.
IVF	63	113.56	50	144	127	2.05	.04
Control	66	108.29	70	159	127	2.04	.04

The MDI of almost 115 for the IVF cases represents the 83rd percentile on the normal curve while the MDI of approximately 111 for the controls represents the 75th percentile (Sattler, 1988, Table BC-1). The PDI of 114 for the IVF children represents the 81st percentile while the PDI of 108 for the controls represents the 69th percentile of the general population (Sattler, 1988, Table BC-1).

Congenital Defects and Cognitive Level

Previous literature from Australia and New Zealand reported that there were associations between birth weight, prematurity, physical anomolies, and below average MDIs and PDIs. In this study there are also some associations. The control with Trisomy 13 was untestable on the Bayley due to visual and hearing impairments. The parent reported that she was probably also severely retarded. This is considered to be an example of a physical defect also involving a cognitive defect with severe retardation being a diagnostic feature of this chromosomal defect. Another association involves the previously cited case with the thoracic myelomeningocele, a congenital abnormality, who was

motorically handicapped and received a PDI of 50. Cognitively this child was within normal limits. The child with the hearing impairment also had an MDI within normal limits.

Effect of Gestational Age and Birth Weight

Prematurity has been associated with lower MDIs and a variety of other complications in the review of the literature both for the general population as well as IVF children. Young (1987) reports that it accounts for 75% of the neonatal mortality; a factor with that lethality deserves careful examination. Prematurity was assessed using both the child's gestational age and birth weight. According to The American Academy of Pediatrics, prematurity is based on a gestational age of less than 38 weeks and a birth weight of less than 2500 grams (Behrman & Vaughan, 1987), and these criteria were used for the analysis of this sample.

Twenty-five per cent of the children in this study were designated as low birth weight (Appendix E). Thirty-one per cent were premature based on a gestational age of 37.5 weeks or less (Appendix F). The national average for prematurity is approximately 8% according to Young (1987), but only 5.7% for whites (Behrman & Vaughan, 1987). Clearly, this sample is different from the general population in this factor with rates three to four times the national average. The sample, however, included 21 sets of twins and 5 sets of triplets

twins and 5 sets of triplets which is an unusually high number of multiple births. Most twins and triplets are born prematurely (Behrman & Vaughan, 1987) so while the sample is unusual it is consistent when all factors are considered. While prematurity is often associated with low socioeconomic status (Behrman & Vaughan, 1987), in this sample it is more likely to be a function of the large number of multiple births.

All IVF cases, regardless of their gestational age, had MDIs of 90 or more (Table 5) which indicates that all had normal cognitive development. No chi-square analysis was necessary since there was no discrepancy. Among the controls, one premature child had an MDI below 90 while two full-term children scored below 90 (Table 6). The chi-square and Fisher's exact test (used for small cell sizes) both yielded nonsignificant differences.

All premature IVF cases also had PDIs of 90 or more (Table 7). The only IVF child with a PDI below 90 was the child with the myelomeningocele, and he was not premature. Three premature controls had PDIs below 90 while only one full-term child scored below 90 (Table 8). Again, both the chi-square and Fisher's exact test yielded non-significant differences.

The relationship between gestational age and MDI was investigated using a Pearson correlation coefficient. The correlations for both cases and controls were non-significant. The results are detailed in Tables 9 and 10.

Table 5

Frequency Count of IVF Cases by Gestational Age

	MDI	
FREQUENCY PERCENT ROW PCT COL PCT	90+	TOTAL
<=37.5 WEEKS	20 31.75 100.00 31.75	20 31.75
>37.5 WEEKS	43 68.25 100.00 68.75	43 68.25
TOTAL	63 100.00	63 100.00

Table 6

Chi-square Comparison of IVF Cases and Controls

Mental Development Index by Gestational Age

	MDI		
FREQUENCY PERCENT ROW PCT COL PCT	0-89	90+	TOTAL
<37.5 WEEKS	1 1.59 5.26 33.33	18 28.57 94.74 30.00	19 30.16
>37.5 WEEKS	2 3.17 4.55 66.67	42 66.67 95.45 70.00	44 69.84
TOTAL	3 4.76	60 95.24	63 100.00

FREQUENCY MISSING = 30

STATISTICS FOR TABLE OF A_GEST BY MDI

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	0.015	0.902
LIKELIHOOD RATIO CHI-SQUARE	1	0.017	0.903
CONTINUITY ADJ. CHI-SQUARE	1	0.000	1.000
MANTEL-HAENSZEL CHI-SQUARE	1	0.015	0.903
FISHER'S EXACT TEST (1-TAIL)			0.616
(2-TAIL)			1.000
PHI		0.015	
CONTINGENCY COEFFICIENT		0.015	
CRAMER'S V		0.015	

Table 7

Chi Square Comparison of IVF Cases on Psychomotor Development Index by Gestational Age

PDI			
FREQUENCY PERCENT ROW PCT COL PCT	0-89	90+	TOTAL
<=37.5 WEEKS	0 0.00 0.00 0.00	20 31.75 100.00 32.26	20 31.75
>37.5 WEEKS	1 1.59 2.33 100.00	42 66.67 97.67 67.74	43 68.25
TOTAL	1 1.59	62 98.41	63 100.00

FREQUENCY MISSING = 19

STATISTICS FOR TABLE OF R_GEST BY PDI

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	0.473	0.492
LIKELIHOOD RATIO CHI-SQUARE	1	0.771	0.380
CONTINUITY ADJ. CHI-SQUARE	1	0.000	1.000
MANTEL-HAENSZEL CHI-SQUARE	1	0.465	0.495
FISHER'S EXACT TEST (1-TAIL)			0.683
(2-TAIL)			1.000
PHI		-0.087	
CONTINGENCY COEFFICIENT		0.086	
CRAMER'S V		-0.087	

Table 8

Chi-square Comparison of Controls on Psychomotor Development Index by Gestational Age

	PDI		
FREQUENCY PERCENT ROW PCT COL PCT	0-89	'90+	TOTAL
<=37.5 WEEKS	3 4.76 15.79 75.00	16 25.40 84.21 27.12	19 30.16
>37.5 WEEKS	1 1.59 2.27 25.00	43 68.25 97.73 72.88	44 69.84
TOTAL	4 6.35	59 93.65	63 100.00

FREQUENCY MISSING = 30

STATISTICS FOR TABLE OF R_GES' BY PDI

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	4.077	0.043
LIKELIHOOD RATIO CHI-SQUARE	1	1.676	0.055
CONTINUITY ADJ. CHI-SQUARE	1	2.121	0.145
MANTEL-HAENSZEL CHI-SQUARE	1	4.013	0.045
FISHER'S EXACT TEST (1-TAIL)			0.078
(2-TAIL)			0.078
PHI		0.254	
CONTINGENCY COEFFICIENT		0.247	
CRAMER'S V		0.254	

Table 9

Pearson Correlation Coefficients on IVF Cases

Mental Development Index/Psychomotor Development Index/

Gestational Age/Maternal Age/Parental Education

PEARSON CORRELATION COEFFICIENTS / PROB > |R| UNDER HO:RHO=0 / NUMBER OF OBSERVATIONS

	MDI	PDI	GESTATN	MOMAGE	MEAN ED
MDI	1.00000 0.0000 61	0.26941 0.0327 61	-0.06770 0.5980 61	0.20207 0.1353 56	0.02753 0.8433 54
PDI	0.26941 0.0327 61	1.00000 0.0000 61	0.02559 0.8422 61	0.14807 0.2761 56	0.01755 0.9068 54
GESTATN GESTATIONAL AGE, WEEKS	-0.06770 0.5980 61	0.02559 0.8422 61	1.00000 0.0000 82	0.24160 0.0294 75	0.12081 0.3086 73
MOMAGE MOTHER AGE AT BABY BIRTH	0.20207 0.1353 56	0.14807 0.2761 56	0.24160 0.0294 75	1.00000 0.0000 75	0.45951 0.0001 73
MEAN ED MEAN PARENT EDUCATION	0.02753 0.8433 54	0.01755 0.9068 54	0.12081 0.3086 73	0.45951 0.0001 73	1.00000 0.0000 73

Table 10

Pearson Correlation Coefficients on Controls

Mental Development Index/Psychomotor Development Index/

Gestational Age/Maternal Age/Parental Education

PEARSON CORRELATION COEFFICIENTS / PROB > |R| UNDER HO:RHO=0 / NUMBER OF OBSERVATIONS

	MDI	PDI	GESTATN	MOMAGE	MEAN ED
MDI	1.00000 0.0000 66	0.44717 0.0002 66	-0.14754 0.2485 63	0.05249 0.6878 61	0.08908 0.4948 61
PDI	0.44717 0.0002 66	1.00000 0.0000 66	0.01277 0.9209 63	0.10644 0.4143 61	0.07777 0.5514 61
GESTATN GESTATIONAL AGE, WEEKS	-0.14754 0.2485 63	0.01277 0.9209 63	1.00000 0.0000 90	0.16147 0.1329 88	0.23917 0.0241 89
MOMAGE MOTHER AGE AT BABY BIRTH	0.05249 0.6878 61	0.10644 0.4143 61	0.16147 0.1329 88	1.00000 0.0000 88	0.16503 0.1244 88
MEAN ED MEAN PARENT EDUCATION	0.08908 0.4948 61	0.07777 0.5514 61	0.23917 0.0241 89	0.16503 0.1244 88	1.00000 0.0000 88

The relationship between gestational age and PDI was likewise investigated using a Pearson correlation coefficient. Again, the correlations for both cases and controls were non-significant; see Tables 9 and 10.

The relationship betwen MDI and birth weight was investigated using a chi-square and Fisher's exact test. All IVF cases, regardless of birthweight, had MDIs of 90 or more (Table 11). No chi-square analysis was necessary because there was no discrepancy. Among the control group, there were three children who scored below 90 (Table 12), but none were premature based on weight. No significant differences were found.

The relationship between birth weight and PDI was also analyzed using the same statistics. One IVF case had a PDI below 90, but it was not premature based on weight (Table 13). The Fisher's exact test indicated no difference. In the control group four children had PDIs below 90; two were premature and two were not (Table 14). The Fisher's exact test was again non-significant.

Table 11

Frequency Count for IVF Cases on Mental Development Index by Birth Weight

MDI / WEIGHTGM	<2500 GM	2500+ GM	TOTAL
0-89	0	0	0
	0.00	0.00	0.00
	0.00	0.00	
90+	16	43	59
	27.12	72.88	100.00
	27.12	72.88	
	100.00	100.00	
TOTAL	16	43	59
	27.12	72.88	100.00

Table 12

Chi-square Comparison of Controls on Mental Development Index by Birth Weight

MDI WEIGHTGM

FREQUENCY / PERCENT / ROW PCT / COL PCT	<2500 GM	2500+ GM	TOTAL
0-89	0	3	3
	0.00	4.84	4.84
	0.00	100.00	
	0.00	6.25	
90+	14	45	59
	22.58	72.58	95.16
	23.73	76.27	
	100.00	93.75	
TOTAL	14	48	62
	22.58	77.42	100.00

FREQUENCY MISSING = 5

STATISTICS FOR TABLE 2 OF MDI BY WEIGHTGM
CONTROLLING FOR CASECNTL=CONTROL

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	0.919	0.338
LIKELIHOOD RATIO CHI-SQUARE	1	1.560	0.209
CONTINUITY ADJ. CHI-SQUARE	1	0.063	0.802
MANTEL-HAENSZEL CHI-SQUARE	1	0.905	0.342
FISHER'S EXACT TEST (1-TAIL)			0.457
(2-TAIL)			1.000
PHI		0.122	
CONTINGENCY COEFFICIENT		0.121	
CRAMER'S V		-0.122	

Table 13

Chi-square Comparison of IVF Cases on Psychomotor Development Index by Birth Weight

POI WEIGHTGM

FREQUENCY / PERCENT / ROW PCT / COL PCT	<2500 GM	2500+ GM	TOTAL
0-89	0	1	1
	0.00	1.69	1.69
	0.00	100.00	
	0.00	2.33	
90+	16	42	58
	27.12	71.19	98.31
	27.59	72.41	
	100.00	97.67	
TOTAL	16	43	59
	27.12	72.88	100.00

FREQUENCY MISSING = 5

STATISTICS FOR TABLE 1 OF POI BY WEIGHTGM
CONTROLLING FOR CASECNTL-CASE

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	0.379	0.538
LIKELIHOOD RATIO CHI-SQUARE	1	0.519	0.471
CONTINUITY ADJ. CHI-SQUARE	1	0.000	1.000
MANTEL-HAENSZEL CHI SQUARE	1	0.372	0.542
FISHER'S EXACT TEST (1-TAIL)			0.729
(2-TAIL)			1.000
PHI		0.080	
CONTINGENCY COEFFICIENT		0.080	
CRAMER'S V		0.080	

Table 14

Chi-square Comparison of Controls on Psychomotor Development Index by Birth Weight

PDI WEIGHTGM

FREQUENCY / PERCENT / ROW PCT / COL PCT	<2500 GM	2500+ GM	TOTAL
0-89	2 3.23 50.00 14.29	2 3.23 50.00 4.17	4 6.45
90+	12 19.35 20.69 85.71	46 74.19 79.31 95.83	58 93.55
TOTAL	14 22.58	48 77.42	62 100.00

FREQUENCY MISSING = 5

STATISTICS FOR TABLE 2 OF PDI BY WEIGHTGM
CONTROLLING FOR CASECNTL-CONTROL

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	1.839	0.175
LIKELIHOOD RATIO CHI-SQUARE	1	1.552	0.213
CONTINUITY ADJ. CHI-SQUARE	1	0.544	0.461
MANTEL-HAENSZEL CHI-SQUARE	1	1.809	0.179
FISHER'S EXACT TEST (1-TAIL)			0.217
(2-TAIL)			0.217
PHI		0.172	
CONTINGENCY COEFFICIENT		0.170	
CRAMER'S V		0.172	

Maternal Age and MDI/PDI

Advanced maternal age is associated with an increased risk for chromosomal defects, primarily Down's syndrome. The mean age for the mothers in this study was 34.47 for cases and 33.17 for controls. Therefore, Pearson correlation coefficients were done to analyze the effect of maternal age on MDI. Since the shape of the bell curves for MDI (Figure 1) and PDI (Figure 2) values in this study resembles a normal distribution, the Pearson statistic was recommended over the Spearman correlation by the study's statistician, E. Chee at Johns Hopkins University, for the grant (personal communication, June 1, 1988). The correlations for cases and controls were non-significant.

The correlation between maternal age and PDI was investigated using the same procedure (Tables 9 and 10). The correlation for both cases and controls was non-significant.

Figure 1

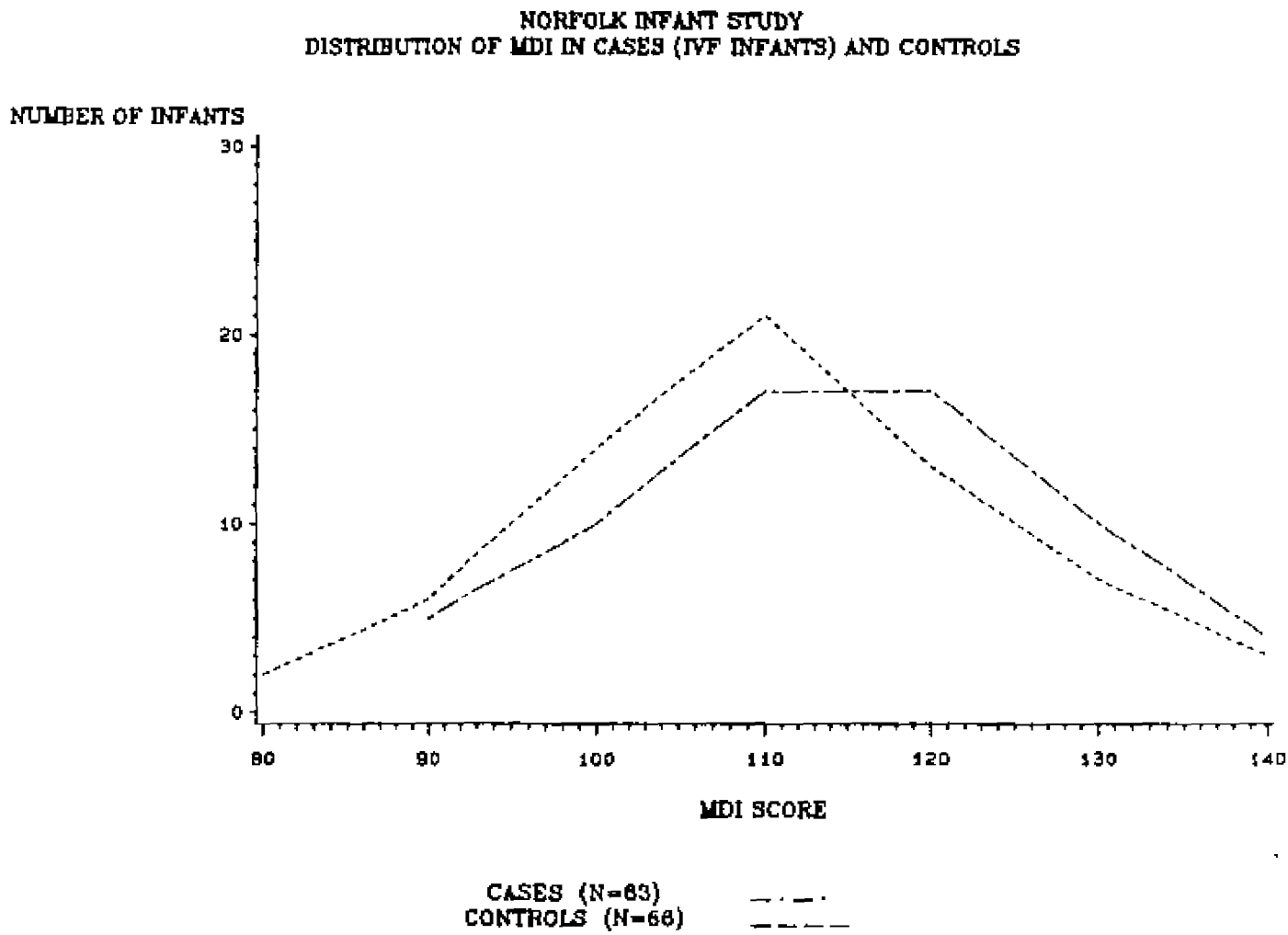
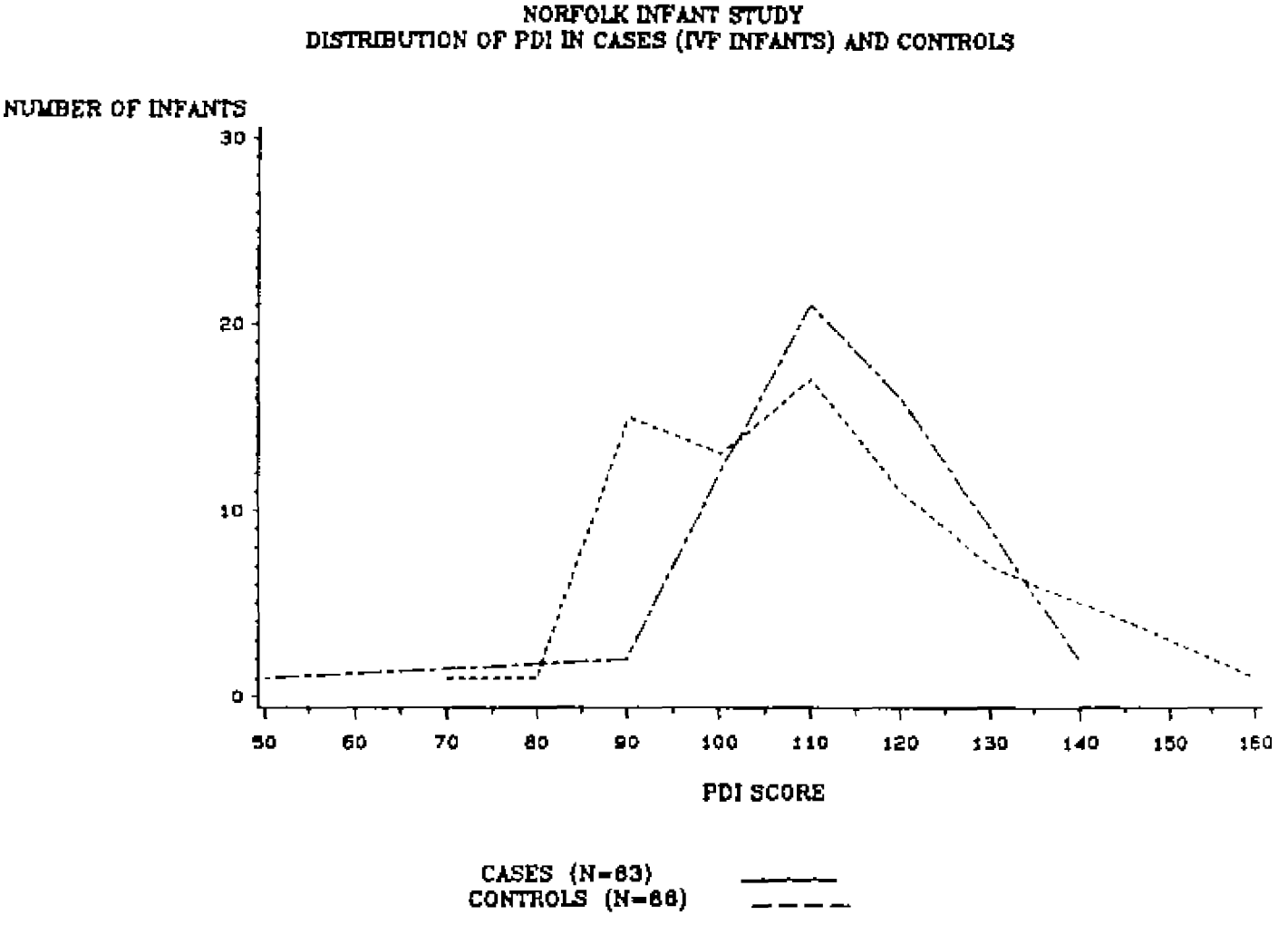

NORFOLK INFANT STUDY
DISTRIBUTION OF MDI IN CASES (IVF INFANTS) AND CONTROLS
NUMBER OF INFANTS
30
20
10
0
80
90
100
110
120
130
140
MDI SCORE
CASES (N=63)
CONTROLS (N=66)

Figure 2


NORFOLK INFANT STUDY
DISTRIBUTION OF PDI IN CASES (IVF INFANTS) AND CONTROLS
NUMBER OF INFANTS
30
20
10
0
50
60
70
80
90
100
110
120
130
140
150
160
PDI SCORE
CASES (N=83)
CONTROLS (N=66)

Effects of Socioeconomic Status

As previously indicated the mean parent education was selected as a measure of socioeconomic status. Pearson correlation coefficients (Tables 9 and 10) were done to analyze the effects of SES on MDIs and PDIs. No relationship was found.

The PDI-SES relationship was also investigated using the Pearson statistic. No relationship was expected, and none was found.

Behavioral Results

Following the psychometric evaluation the examiner completed the Infant Behavior Record in its entirety to document the qualitative aspects of the child's performance. It was completed for the two children who would not cooperate even though there were no psychometric scores for them.

Chi-squares were run on all thirty variables (Tables 15 to 44 in Appendix) of the Infant Behavior Record to analyze the differences, if any, between cases and controls. In many cases there were cell sizes of less than five because many of the variables were measured on 9-point scales. This casts some doubt on whether the chi-square results are valid. The variable with its probability value are listed here in the order they appear in the test booklet.

VARIABLE	PROBABILITY
Respond to others	.725
Respond to tester	.300
Respond to mother	.835
Cooperation with tester	.719
Fearful	.128
Tension	.670
Happiness	.307
Respond to objects	.278
Plays imaginatively	.587
Object attachment	.486
Goal directedness	.302
Attention span	.375
Endurance	.653
Activity	.503
Reactivity	.099
Responds to sights	.501
Listens	.427
Vocal sounds*	.015
Banging of objects	.954
Manipulates with hands	.309
Body motion	.325
Thumb sucking	.218
Pacifier sucking	.787
Mouthing toys	.793
Energy level*	.027
Gross motor coordination	.090

Fine motor coordination	.156
Examiner's judgement of test	.795
Deviant behavior	.448
General evaluation	1.000

Of the thirty chi-square results there were only two variables where the differences between the two groups approached the significance level established for this study. The IVF children were more vocal (number 18) and had higher energy levels (number 25).

The vocalization variable was measured on a 9-point scale with the higher numbers indicating excessive (Bayley's term) vocalization. Only IVF children received ratings of seven or more, and there were ten who did. The chi-square value is .015. There were 55% of the cells, however, which had counts of less than five which casts doubt on the validity of the statistic.

The energy level variable was measured on a 5-point scale with the higher numbers indicating higher levels. Ten IVF cases received a rating of 4 while only five controls did so. Three IVF cases received a rating of 5 while no controls were rated that high. The chi-square value for this variable is .027, but because 40% of the cells had counts of less than five this statistic may also be invalid.

CHAPTER 5

Overview

Lancaster summarized the risks of in vitro fertilization in 1985 this way:

> Women who become pregnant after in vitro fertilisation (sic) are usually older than their peers who conceive naturally, have atypical reproductive histories, and have been managed by novel techniques. Likewise, their fetuses have initially developed and been nurtured in potentially hazardous conditions, being exposed to various physical manipulations, to a possibly inadequately prepared uterine environment, and often to various hormonal and drug regimens. Hence it might be expected that outcomes of pregnancy resulting from in vitro fertilisation would differ from those after natural conceptions, especially when the initial experiences of in vitro fertilisation units are being examined (p. 1162).

This research was sponsored by The National Institute of Child Health and Human Development in order to address the risk(s), both physical and psychological, of the IVF process to the child. The physical and psychological development of a child is the result of many factors, some known and some

unknown. Bayley (1970) addressed the prenatal and paranatal "environments" that could result in damage to the organism and its mental abilities (p. 1164), and the IVF process does alter these prenatal environments. The review of IVF literature cites an unusually high rate of embryonic loss, chromosomal defects in abortuses, prematurity, and cesarian section deliveries. The research from Australia and New Zealand found more heart and spinal defects than is seen in that normal population (Lancaster, 1987). Early psychological studies from Australia and New Zealand by Mushin and Yovich found, however, that the children were developing normally in the cognitive, motor, and behavioral domains. The children had average or higher MDIs or General Quotients except in a few cases which were explained by physical defects or prematurity. While this was reassuring the samples were small, the children were still very young, and there were no control groups. Also, there had yet to be a follow-up study from the Western hemisphere, either the United States or England. All research to date has specified that larger numbers and a control group were needed.

This study attempted to address these issues in its design. There were 178 children evaluated for physical abnormalities, and 131 were evaluated psychologically; these are large numbers relative to the previous follow-up studies. Another strength of the study was that all children were seen by the same examiners (except for a small

number of cardiac evaluations). This minimizes the problem of inter-rater reliability. The recording of findings was standardized for consistency. The examinations were conducted in the same physical space at Children's Hospital of The King's Daughters for all children which controls one more variable.

A very important feature of this study is the quality of the control group. While a normal obstetric control group is less than ideal as discussed by Lancaster (1987) from an epidemiological standpoint, it is legitimate to compare the groups from a consumer standpoint. The couples seeking to have a child by this method are presumably seeking a normal child, and the question is whether the IVF technology results in a reasonable risk for a normal, healthy child. The control group closely matched the IVF sample on all specified variables: maternal age, child age, number of births/pregnancy, gender, race, and socioeconomic status. The procedures for obtaining these matches were carefully arranged by an epidemiologist. While it was not feasible to obtain the matches from the case's hometown (which would have been a preferable design), the geographical area covered a 100 mile radius of the testing site and more in the case of triplets.

CONCLUSIONS

The Population

Several factors emerged which identify the IVF cases and their parents as different from the general population. First, the mothers are older than the general obstetric patient, but they are part of the trend toward delaying childbirth. For these women the delay may be involuntary while other infertility treatments are attempted, but many of these women gave birth to their first child in their early to mid-thirties.

Second, the IVF population is almost entirely white. Only one black child was identified out of 83 cases, or 1.2%. There was some ethnic diversity with Greek, Indian, and Canadian families participating in this study.

Third, the IVF population contains many more multiple births than the general population. With 13 sets of twins and three sets of triplets in 110 births, the rate is close to sixteen times the normal rate. This is consistent with the Australia and New Zealand findings and the procedure of inducing multiple egg production, fertilization, and implantation. Since multiple births are usually premature, this factor carries with it many risks including: low birth weight, increased mortality, congenital anomalies, and anoxic damage. This study looked at prematurity in terms of both gestational age and birth weight because this factor carries such risk. Since none of the IVF cases had MDIs below 90 this study failed to find any increased risk for

the IVF children due to multiple births and/or prematurity. According to Behrman and Vaughan congenital malformations are more common in premature infants; "those with the slowest intrauterine growth rates have the highest incidence of malformations" (1987, p. 346). Ward and DeWitte, however, report that a healthy premature infant weighing more than 1700 grams can have the same outcome as a full-term infant, "including normal intellectual function" (1987, p. 550). The birth weight of seven children was not recorded, but while 25% of 124 children had birthweights of 2500 grams or less, only 7% were below 1700 grams. Ward and DeWitte's optimistic prognosis for the larger premature infant may be the factor that accounts for the positive outcome for this group despite the body of literature which documents the grave risks associated with prematurity.

Fourth, the IVF children are born to an affluent and well educated group of parents. The control group was the better educated, but both groups surpassed the national figures for college educations. The IVF group reported higher family incomes, but this information was not collected in 17 instances which may have disguised the magnitude of the discrepancy. The data regarding education was missing in only nine instances. This affluence is expected since the IVF procedure costs approximately $5,000 per attempt, and it is often not covered by insurance on the grounds that it is an experimental treatment.

CONCLUSIONS

Research Questions

Question One

The first question was whether the IVF infants differed from their matched controls on the Mental and Psychomotor Scales of the Bayley. The T-tests (Tables 3, 4, and Appendix D) indicate that they do not differ significantly according the confidence level established for the study, p=.01. The IVF children were higher on both scales, but the difference was only 3.6 points on the Mental Scale and 5.3 points on the Psychomotor Scale. The T-test value for the MDI is 1.56 (p=.12), and for the PDI it is 2.05 (p=.04). The null hypothesis is accepted which stated that there was no difference between the groups. Even if this is incorrect, the IVF children have more positive findings than the control group. The potential risks did not have a detrimental effect on these children, cognitively or motorically.

Question Two

The second question was whether the groups differ from the normative data of the Bayley Scales. The Bayley standard scores are based on a mean of 100 and standard deviations of 16. Both groups are above the mean on both scales. The IVF MDI mean of 114.97 represents the 83rd percentile of the general population. The control MDI mean of 111.38 represents the 75th percentile of the general

population. The PDIs for the IVF cases and controls represent the 81st and 69th percentiles respectively (Sattler, 1988, Table BC-1). This suggests that these groups are different from the general population of infants and in a positive way. Stein (1985) reported in a follow-up study of 50,000 children at seven years of age, "As we expected, the older the mother, the higher was the I.Q." (p. 338). She also suggests that there is a strong relationship between the mother's education and the child's measured intelligence. Other factors suggested are the age-related variables of wisdom, judgement, restraint, and even economic security. These are hypotheses which should be researched in the future, and it is unknown whether these are the factors associated with these results. While the children in that research are much older than these in the IVF research, the finding related to maternal age deserves consideration. Bayley (1937) believed the increasing correlation between mental abilities and socioeconomic factors to be a function of both education and genetic factors, but the correlations are very modest in the sensorimotor period.

Golden and Birns (1976) in their chapter on social class and infant intelligence write

> ...we would have to conclude that, in general, social class differences in infant or sensorimotor intelligence probably do not exist. Clear-cut, consistent, pervasive social class differences in

> intellectual performance on a variety of measures emerge somewhere between 18 and 24 months of age. Since SES differences in cognitive development first manifest themselves during a period of rapid language growth, it is reasonable to assume that these differences may be due to language...While sensorimotor intelligence may be the foundation for later intelligence, as Piaget believes, there is no reason to assume that the rate of cognitive development or intellectual competence of normal children should be the same on the sensorimotor and the verbal levels (p. 343).

They did a longtitudinal study in the early 1970s on white males beginning at 24 months of age using the Bayley. They found a 21-point IQ difference (92 versus 113) between two groups where membership in a group was based on maternal education; the high education group consisted exclusively of mothers who had a college degree. They did not expect the difference to be so large, and they attributed the difference to differences in parental education. This study has several similarities to this IVF research: age of the children, race, instrumentation, and results. The major difference is in the use of boys only; while the IVF and control groups are 7-8 months younger on average, this is not considered a major difference. This author presumes that Golden and Birns have substituted IQ for MDI because it is a more familiar term, but the high education group

obtained a mean IQ of 113 while the IVF group had a mean MDI of 115 (rounded off) and the control group mean was 111. Both groups had well educated parents, similar to Golden and Birn's groups.

Less can be said about the significance of the higher PDIs for both groups in this research because these scores are seldom reported in the literature. It is this author's impression that the Psychomotor Scale is administered far less often than the Mental Scale. According to Sattler (1988), the correlation between the MDI and PDI decreases with age and so they are considered to be measuring different abilities. It would not be assumed that high MDIs would automatically infer high PDIs. In light of the above average results for both groups, there would be no reason for concern regarding their motor competence.

Question Three

The third research question addressed the association between risk factors, especially prematurity and multiple births, and the IVF child. None of the IVF children had MDIs below 90. No association was found between low MDIs and congenital anomalies or prematurity. In light of the reports from Australia and New Zealand associating lower scores with physical findings, this is considered a very positive outcome. There was a child with a thoracic myelomeningocele who was motorically handicapped (PDI=50),

but he demonstrated no cognitive impairment. Even the IVF child with the mild hearing loss performed within the average range. There were three controls with MDIs below 90, but these were not associated with physical findings either.

Considering that there were so many children who qualified as premature based on gestational age or birth weight and that prematurity is associated with physical as well as cognitive defects, it is curious that this study would not find some association. One possibility is that at the socioeconomic level of most of these families there would be early and comprehensive obstetric care. These are also women who would be conscientious about their behavior during pregnancy as it would affect their child (i.e. diet, exercise, rest, smoking, etc.). These factors would mitigate the impact of prematurity and encourage the birth of a healthy premature child.

Question Four

The fourth question addressed whether the IVF cases differed from the controls on behavioral characteristics. Haviland (1976) in a chapter on affect and intelligence asserts that affective states such as enjoyment and fearfulness impact not only the child's test performance but also on their approach to the world in general. Behavioral attributes are difficult to interpret because increased body tension, for example, may be appropriate if attempting a

challenging task but inappropriate for a routine task. She indicates that positive affect during testing is one of the better predictors of later intelligence. While she expresses a variety of reservations about the Bayley Infant Behavior Record, her chapter relies heavily on it as an example of the role of affect in infant intelligence. She interprets Piaget as using "affect to infer intelligence" (1976, p. 360). His references to a child's curiosity, excitement, disappointment, surprise, and rage are integrated into his theorizing about that child's cognitive development. For example, a child would be disappointed only if there was an expectation which would indicate that the child had drawn a conclusion, a cognitive act. The affective quality of the IVF children was considered a worthwhile research question in keeping with Sokoloff's concern for the emotional welfare of these children. It was also seen as a means to assess the possibility that the parenting of IVF children would be different and result in different behavioral patterns in these children.

The chi-square tests run on all thirty measures failed to identify any differences significant at the .01 level. Two, however, approached significance. Vocal sounds had a probability level of .015, and energy level had a probability level of .027. By virtue of having done 30 analyses there is a chance that some would be significant simply because there were so many.

The vocalization factor has received some attention in the literature regarding infant assessment, and it is considered a positive finding. Matheny (1974) included it in his cluster of behaviors relating to "persistence and concentrated interest ...because of the known relation between infants' utterances and intellectual skills" (p. 699). It is associated in girls more than boys with prediction of later verbal competence. Honzik (1976) cites research by Moore (1968) in England along with Kagan (1971) and McCall (1972) in the United States as finding "special salience for females that it does not connote for males with respect to predicting later mental test performance" (p. 73). Golden and Birns (1976) assert that social classes differ in their communication styles with children, and this may be an advantage that middle class children have on standardized tests generally. These communication styles become incorporated into the child's cognitive development and are reflected in their performance on tests such as the Bayley especially as the tests become more language oriented and less sensorimotor. This is widely regarded as the factor which accounts for the increased predictive validity of infant tests around 24 months. The parent-child interaction may also play a role in vocalization. These IVF parents may be extraordinarily invested in their children since they expended so much time, energy, and money in having their own biological child. This may be reflected in a different type of interaction, perhaps verbal, with their

child than is normally seen. This study did not attempt to study to parent-child interaction, but it is considered to be a possibility.

It is more difficult to interpret the higher energy level finding of the IVF children. In the literature review this author did not find Energy Level to be in any of the cluster analyses suggested by some authors nor is it reported as a factor unto itself. It is this author's clinical experience that some children become energized by novelty and/or fatigue. In many cases the IVF children had traveled across time zones which disrupted their schedules, slept in hotels without some of their usual comforts or routines, and were fed different foods in restaurants. While many of parents went to great lengths to bring the comforts of home with them, air travel and hotels were nevertheless novel. The controls were obtained locally and did not experience these disruptions. All of these disruptions in their routines could be expected to have some behavioral manifestation, perhaps an energizing one.

It would be a very tedious process to interpret the results of each behavior variable because there is no consistency to the numerical ratings. In addition, the computer printout issued the caveat on many of the variables that the cell sizes were small which would invalidate the chi-square test. When no significant differences between the IVF cases and controls have been identified, beyond the

two already discussed, a discussion of each item is not considered productive.

LIMITATIONS

This research is based upon the IVF infants conceived at only one location, Norfolk, Virginia. At the time that the grant was awarded The National Institute of Child Health and Human Development was interested in obtaining large numbers of children for study. The Jones Institute was this country's most successful IVF program and the only one which could provide more than 40 children for study. The benefits of controlling the variables of evaluation team and location were considered more desirable than using different teams in different cities or moving the team and being unable to control the physical plant factors. These results reflect the outcome for one center only, and there are now many sites where IVF is being offered. The outcomes for other centers may be different.

Ideally the matches would have been obtained from the cases' hometowns. The epidemiologist was concerned that there may be geographical factors related to infertility which would be missed by restricting the geography of the control group. Economically this was infeasible.

The team also considered the desirability of having a second control group which would have a history of infertility yet achieved a successful pregnancy without IVF.

This would have assessed the impact of infertility alone without being commingled with IVF procedures. Identifying this group would have been difficult and would have increased the cost of the study; this idea was reluctantly abandonned. If the IVF results had indicated that the children were experiencing higher than normal abnormalities of any kind, then this control group would assume more importance and should be included.

These IVF children were born to parents who pioneered the unknown and ethically/morally clouded domain of non-coital reproduction. They were risk takers. Some risked the displeasure of their families and kept the infant's method of conception a secret. They risked large amounts of money because there was no assurance of success. They are well educated and affluent. While IVF is taken for granted today, newspapers reported the births of many of these children due to their novelty. These parents represent a select population and may not represent the IVF participants of today or the future. If IVF becomes more available financially and geographically to larger numbers these results may not be representative.

This study represents only the beginning of the follow-up on these children. The results are encouraging because most major and minor abnormalities would have been identified in the course of this multi-disciplinary evaluation, even at this young age. These psychological results do not predict the eventual cognitive, motor, or

behavioral characteristics of these children. Sokoloff's questions regarding the psychological welfare of these children when they are aware of their history have not been answered. Hubble's concern for their offsprings' well-being cannot be answered for at least another decade.

RECOMMENDATIONS

This research should be replicated by other IVF centers. While the methodology used by the Joneses has been widely disseminated and used as a model it cannot be assumed that all centers are using the same methodology or obtaining the same results. This design could be improved by including the infertile control group and by geographically matching the control group(s).

Long-term follow-up is strongly recommended. The Bayley is an excellent infant psychometric instrument, but it lacks predictive validity. The IVF children should be followed into adulthood to assess their outcomes in the broadest sense. This should include both intellectual and personality assessments. Their emotional adjustment should be investigated. Kochakian (1988) reviewed a book entitled The Too Precious Child by Drs. L. H. Williams (psychiatrist) and H. S. Berman (pediatrician), and L. Rose. Parents are at risk if they have delayed becoming parents, had difficulty conceiving or delivering a child, or have fewer children. These are only a few of the risk factors, but

these are descriptive for most of the IVF parents. Such parents are at risk for overinvolvement, and there may be problems with separation, expectations, and peer relationships. Parent-child issues may be reflected in the ability of IVF children to parent effectively. Will they feel stigmatized and seek to keep their conception a secret? Will reluctant families have come to accept them? Will they struggle with the label "test tube babies"? These are some of the issues Sokoloff alludes to when he asks, "How is he/she doing physically and emotionally?" (1987, p. 11). These are important issues in their ultimate adjustment, and there are no answers today.

SUMMARY

The IVF sample evaluated in this study was found to be within normal limits physically with no increased risk for congenital malformations. The psychological evaluation found no significant differences between the IVF children and the matched controls on any of the variables. While a large percentage were at risk due to their prematurity, no risk was realized in either their physical or psychological outcomes. Both groups performed above average on both the Mental and Psychomotor Scales of the Bayley Scales of Infant Development compared with the national norms, and the IVF children received higher scores than did the controls. These findings suggest that the IVF process does not result

in a higher risk for congenital anomalies or psychological deficits in the toddler. The IVF children progress through the early Piaget-defined stages in the same way as their normally conceived peers. Future psychological development cannot, however, be predicted from these results.

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APPENDIX

Table 15

Chi-square Comparison of IVF Cases and Controls on Responsiveness to Others

CASECNTL S1(RESPOND TO OTHERS)

FREQUENCY / PERCENT / ROW PCT / COL PCT	5	6	7	8	9	TOTAL
CASE	0	10	39	5	9	63
	0.00	7.63	29.77	3.82	6.87	48.09
	0.00	15.87	61.90	7.94	14.29	
	0.00	52.63	47.56	50.00	50.00	
CONTROL	2	9	43	5	9	68
	1.53	6.87	32.82	3.82	6.87	51.91
	2.94	13.24	63.24	7.35	13.24	
	100.00	47.37	52.44	50.00	50.00	
TOTAL	2	19	82	10	18	131
	1.53	14.50	62.60	7.63	13.74	100.00

STATISTICS FOR TABLE OF CASECNTL BY S1

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	4	2.060	0.725
LIKELIHOOD RATIO CHI-SQUARE	4	2.830	0.587
MANTEL-HAENSZEL CHI-SQUARE	1	0.142	0.706
PHI		0.125	
CONTINGENCY COEFFICIENT		0.124	
CRAMER'S V		0.125	

Table 16

Chi-square Comparison of IVF Cases and Controls on Responsiveness to Tester

CASECNTL S2(RESPOND TO TESTER)

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	4	5	TOTAL
CASE	5	10	25	20	3	63
	3.82	7.63	19.08	15.27	2.29	48.09
	7.94	15.87	39.68	31.75	4.76	
	71.43	41.67	41.67	55.56	75.00	
CONTROL	2	14	35	16	1	68
	1.53	10.69	26.72	12.21	0.76	51.91
	2.94	20.59	51.47	23.53	1.47	
	28.57	58.33	58.33	44.44	25.00	
TOTAL	7	24	60	36	4	131
	5.34	18.32	45.80	27.48	3.05	100.00

STATISTICS FOR TABLE OF CASECNTL BY S2

STATISTIC	DF	VALUE	PROB
CHI SQUARE	4	4.880	0.300
LIKELIHOOD RATIO CHI-SQUARE	4	4.974	0.290
MANTEL-HAENSZEL CHI-SQUARE	1	0.372	0.542
PHI		0.193	
CONTINGENCY COEFFICIENT		0.190	
CRAMER'S V		0.193	

Table 17

Chi-square Comparison of IVF Cases and Controls on Responsiveness to Mother

CASECNTL S3(RESPOND TO MOTHER)

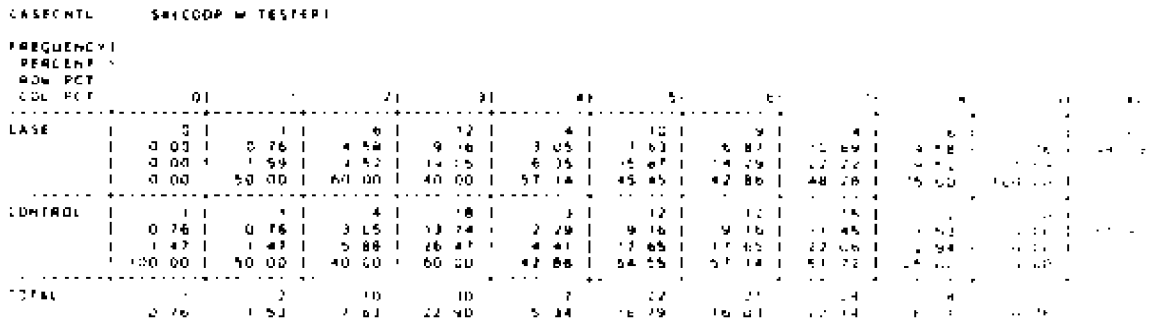
FREQUENCY / PERCENT / ROW PCT / COL PCT	3	4	5	TOTAL
CASE	8	31	24	63
	6.11	23.66	18.32	48.09
	12.70	49.21	38.10	
	50.00	45.59	51.06	
CONTROL	8	37	23	68
	6.11	28.24	17.56	51.91
	11.76	54.41	33.82	
	50.00	54.41	48.94	
TOTAL	16	68	47	131
	12.21	51.91	35.88	100.00

STATISTICS FOR TABLE OF CASECNTL BY S3

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	2	0.360	0.835
LIKELIHOOD RATIO CHI-SQUARE	2	0.360	0.835
MANTEL-HAENSZEL CHI-SQUARE	1	0.085	0.771
PHI		0.052	
CONTINGENCY COEFFICIENT		0.052	
CRAMER'S V		0.052	

Table 18

Chi-square Comparison of IVF Cases and Controls on Cooperativeness with Tester



CASECNTL $*$ COOP W TESTER

FREQUENCY / PERCENT / ROW PCT / COL PCT	01		2	3	4	5	6	7	8	9	
CASE	0	1	6	12	4	10	9	4	6	2	
	0.00	0.76	4.58	9.16	3.05	1.63	6.87	11.69	4.58	1.53	
	0.00	1.59	3.53	14.12	6.35	15.87	14.29	12.70	9.52	3.17	
	0.00	50.00	60.00	40.00	57.14	45.45	42.86	44.44	75.00	100.00	
CONTROL	1	1	4	18	3	12	12	5	2	0	
	0.76	0.76	3.05	13.74	2.29	9.16	9.16	11.45	1.53	0.00	
	1.47	1.47	5.88	26.47	4.41	17.65	17.65	7.35	8.82	0.00	
	100.00	50.00	40.00	60.00	42.86	54.55	57.14	55.56	25.00	0.00	
TOTAL	1	2	10	30	7	22	21	9	8	2	
	0.76	1.53	7.63	22.90	5.34	16.79	16.03	6.87	6.11	1.53	

STATISTICS FOR TABLE OF CASECNTL BY COOP

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	9	16.4106	0.0588
LIKELIHOOD RATIO CHI-SQUARE	9	17.0754	0.0478
MANTEL-HAENSZEL CHI-SQUARE	1	0.8859	0.3465
PHI		0.2778	
CONTINGENCY COEFFICIENT		0.2132	
CRAMER'S V		0.2778	

Table 19

Chi-square Comparison of IVF Cases and Controls on Fearfulness

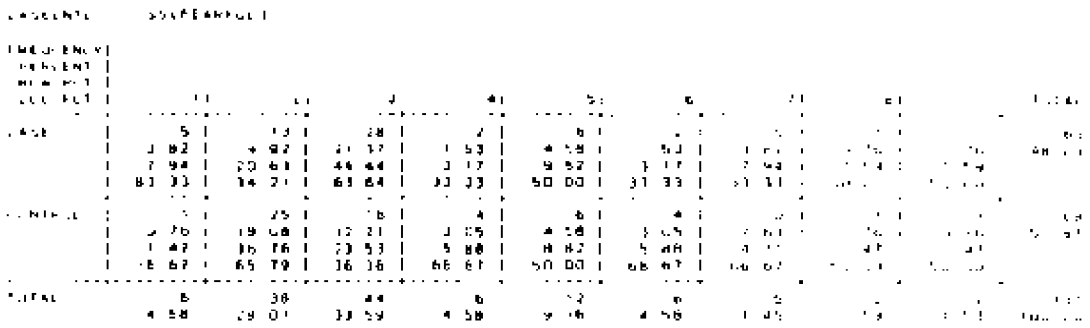


Table 20

Chi-square Comparison of IVF Cases and Controls on Tenseness of Body

CASECNTL SS(TENSE)

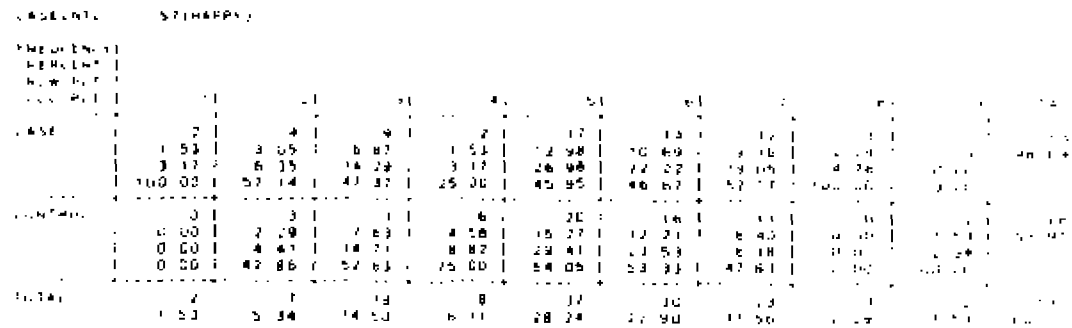
FREQUENCY / PERCENT / ROW PCT / COL PCT	2	3	4	5	6	7	TOTAL
CASE	1	14	28	18	1	1	63
	0.76	10.69	21.37	13.74	0.76	0.76	48.09
	1.59	22.22	44.44	28.57	1.59	1.59	
	100.00	56.00	45.90	43.90	50.00	100.00	
CONTROL	0	11	33	23	1	0	68
	0.00	8.40	25.19	17.56	0.76	0.00	51.91
	0.00	16.18	48.53	33.82	1.47	0.00	
	0.00	44.00	54.10	56.10	50.00	0.00	
TOTAL	1	25	61	41	2	1	131
	0.76	19.08	46.56	31.30	1.53	0.76	100.00

STATISTICS FOR TABLE OF CASECNTL BY SS

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	5	3.193	0.670
LIKELIHOOD RATIO CHI-SQUARE	5	3.964	0.555
MANTEL-HAENSZEL CHI-SQUARE	1	0.457	0.499
PHI		0.156	
CONTINGENCY COEFFICIENT		0.154	
CRAMER'S V		0.156	

Table 21

Chi-square Comparison of IVF Cases and Controls on Degree of Happiness



STATISTICS FOR TABLE OF CASE/CTL BY ...

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	8	9.454	0.307
LIKELIHOOD RATIO CHI-SQUARE	8	7.224	0.512
MANTEL-HAENSZEL CHI-SQUARE	1	0.031	0.861
PHI		0.268	
CONTINGENCY COEFFICIENT		0.257	
CRAMER'S V		0.268	

Table 22

Chi-square Comparison of IVF Cases and Controls on Responsiveness to Objects

CASECNTL SB(RESPOND TO OBJECTS)

FREQUENCY / PERCENT / ROW PCT / COL PCT	3	4	5	6	7	8	9	TOTAL
CASE	1	0	9	21	30	1	1	[illegible]
	0.76	0.00	6.87	16.03	22.90	0.76	0.76	[illegible]
	1.59	0.00	14.29	33.33	47.62	1.59	1.59	
	100.00	0.00	42.86	55.26	50.85	20.00	25.00	
CONTROL	0	3	12	17	29	4	3	[illegible]
	0.00	2.29	9.16	12.98	22.14	3.05	[illegible]	[illegible]
	0.00	4.41	17.65	25.00	42.65	5.88	4.41	
	0.00	100.00	57.14	44.74	49.15	80.00	75.00	
TOTAL	1	3	21	38	59	5	4	[illegible]
	0.76	2.29	16.03	29.01	45.04	3.82	[illegible]	[illegible]

STATISTICS FOR TABLE OF CASECNTL BY SB

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	6	7.487	0.278
LIKELIHOOD RATIO CHI-SQUARE	6	9.197	0.164
MANTEL-HAENSZEL CHI-SQUARE	1	0.068	0.795
PHI		0.239	
CONTINGENCY COEFFICIENT		0.233	
CRAMER'S V		0.239	

Table 23

Chi-square Comparison of IVF Cases and Controls on Imaginative Play

CASECNTL S9(PLAYS IMAGINATIVELY)

FREQUENCY / PERCENT / ROW PCT / COL PCT	YES	NO	TOTAL
CASE	3	60	63
	2.29	45.80	48.09
	4.76	95.24	
	60.00	47.62	
CONTROL	2	66	68
	1.53	50.38	51.91
	2.94	97.06	
	40.00	52.38	
TOTAL	5	126	131
	3.82	96.18	100.00

STATISTICS FOR TABLE OF CASECNTL BY S9

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	0.295	0.587
LIKELIHOOD RATIO CHI-SQUARE	1	0.296	0.586
CONTINUITY ADJ. CHI-SQUARE	1	0.008	0.931
MANTEL-HAENSZEL CHI-SQUARE	1	0.293	0.588
FISHER'S EXACT TEST (1-TAIL)			0.464
(2-TAIL)			0.671
PHI		0.047	
CONTINGENCY COEFFICIENT		0.047	
CRAMER'S V		0.047	

Table 24

Chi-square Comparison of IVF Cases and Controls on Object Orientation

CASECNTL S10(OBJECT ATTACHMNT)

FREQUENCY / PERCENT / ROW PCT / COL PCT	YES	NO	TOTAL
CASE	9	54	63
	6.87	41.22	48.09
	14.29	85.71	
	56.25	46.96	
CONTROL	7	61	68
	5.34	46.56	51.91
	10.29	89.71	
	43.75	53.04	
TOTAL	16	115	131
	12.21	87.79	100.00

STATISTICS FOR TABLE OF CASECNTL BY S10

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	0.486	0.486
LIKELIHOOD RATIO CHI-SQUARE	1	0.486	0.486
CONTINUITY ADJ. CHI-SQUARE	1	0.185	0.667
MANTEL-HAENSZEL CHI-SQUARE	1	0.482	0.487
FISHER'S EXACT TEST (1-TAIL)			0.333
(2-TAIL)			0.596
PHI		0.061	
CONTINGENCY COEFFICIENT		0.061	
CRAMER'S V		0.061	

Table 25

Chi-square Comparison of IVF Cases and Controls on Goal Directedness

CASECNTL SH(GOAL DIRECTED)

FREQUENCY / PERCENT / ROW PCT / COL PCT	2	3	4	5	6	7	8	9	TOTAL
CASE	1	3	14	29	9	7	0	0	[illegible]
	0.76	2.29	10.69	22.14	6.87	5.34	0.00	0.00	[illegible]
	1.59	4.76	22.22	46.03	14.29	11.11	0.00	0.00	
	100.00	25.00	43.75	52.73	52.94	63.64	0.00	0.00	
CONTROL	0	9	18	26	8	4	1	2	[illegible]
	0.00	6.87	13.74	19.85	6.11	3.05	0.76	1.53	[illegible]
	0.00	13.24	26.47	38.24	11.76	5.88	1.47	2.94	
	0.00	75.00	56.25	47.27	47.06	36.36	100.00	100.00	
TOTAL	1	12	32	55	17	11	1	2	[illegible]
	0.76	9.16	24.43	41.98	12.98	8.40	0.76	1.53	[illegible]

STATISTICS FOR TABLE OF CASECNTL BY SH

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	7	8.362	0.302
LIKELIHOOD RATIO CHI-SQUARE	7	10.046	0.186
MANTEL-HAENSZEL CHI-SQUARE	1	0.391	0.532
PHI		0.253	
CONTINGENCY COEFFICIENT		0.245	
CRAMER'S V		0.253	

Table 26

Chi-square Comparison of IVF Cases and Controls on Attention Span

CASECNTL S12(ATTENTION SPAN)

FREQUENCY / PERCENT / ROW PCT / COL PCT	2	3	4	5	6	7	8	9	TOTAL
CASE	1	1	2	27	18	13	0	[illegible]	[illegible]
	0.76	0.76	1.53	20.61	13.74	9.92	0.00	[illegible]	[illegible]
	1.59	1.59	3.17	42.86	28.57	20.63	0.00	[illegible]	
	100.00	25.00	33.33	50.00	41.86	68.42	0.00	[illegible]	
CONTROL	0	3	4	27	25	6	1	2	[illegible]
	0.00	2.29	3.05	20.61	19.08	4.58	0.76	[illegible]	[illegible]
	0.00	4.41	5.88	39.71	36.76	8.82	1.47	[illegible]	
	0.00	75.00	66.67	50.00	58.14	31.58	100.00	[illegible]	
TOTAL	1	4	6	54	43	19	1	[illegible]	[illegible]
	0.76	3.05	4.58	41.22	32.82	14.50	0.76	[illegible]	[illegible]

STATISTICS FOR TABLE OF CASECNTL BY S12

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	7	7.539	0.375
LIKELIHOOD RATIO CHI-SQUARE	7	8.433	0.296
MANTEL-HAENSZEL CHI-SQUARE	1	0.226	0.635
PHI		0.240	
CONTINGENCY COEFFICIENT		0.233	
CRAMER'S V		0.240	

Table 27

Chi-square Comparison of IVF Cases and Controls on Endurance

CASECNTL S13(ENDURANCE)

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	4	5	6	7	9	TOTAL
CASE	1	1	7	3	27	10	13	1	
	0.76	0.76	5.34	2.29	20.61	7.63	9.92	0.76	
	1.59	1.59	11.11	4.76	42.86	15.87	20.63	1.59	
	100.00	100.00	50.00	37.50	54.00	38.46	48.15	25.00	
CONTROL	0	0	7	5	23	16	14	3	
	0.00	0.00	5.34	3.82	17.56	12.21	10.69	2.29	
	0.00	0.00	10.29	7.35	33.82	23.53	20.59	4.41	
	0.00	0.00	50.00	62.50	46.00	61.54	51.85	75.00	
TOTAL	1	1	14	8	50	26	27	4	
	0.76	0.76	10.69	6.11	38.17	19.85	20.61	3.05	

STATISTICS FOR TABLE OF CASECNTL BY S13

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	7	5.058	0.653
LIKELIHOOD RATIO CHI-SQUARE	7	5.888	0.553
MANTEL-HAENSZEL CHI-SQUARE	1	1.348	0.246
PHI		0.196	
CONTINGENCY COEFFICIENT		0.193	
CRAMER'S V		0.196	

Table 28

Chi-square Comparison of IVF Cases and Controls on Gross Bodily Movement

CASECNTL S14(ACTIVITY)

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	3	4	5	6	7	8	9	TOTAL
CASE	1	4	4	38	8	5	2	1	63
	0.76	3.05	3.05	29.01	6.11	3.82	1.53	0.76	48.09
	1.59	6.35	6.35	60.32	12.70	7.94	3.17	1.59	
	100.00	36.36	44.44	53.52	38.10	38.46	100.00	33.33	
CONTROL	0	7	5	33	13	8	0	2	68
	0.00	5.34	3.82	25.19	9.92	6.11	0.00	1.53	51.91
	0.00	10.29	7.35	48.53	19.12	11.76	0.00	2.94	
	0.00	63.64	55.56	46.48	61.90	61.54	0.00	66.67	
TOTAL	1	11	9	71	21	13	2	3	131
	0.76	8.40	6.87	54.20	16.03	9.92	1.53	2.29	100.00

STATISTICS FOR TABLE OF CASECNTL BY S14

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	7	6.316	0.503
LIKELIHOOD RATIO CHI-SQUARE	7	7.501	0.379
MANTEL-HAENSZEL CHI-SQUARE	1	0.116	0.733
PHI		0.220	
CONTINGENCY COEFFICIENT		0.214	
CRAMER'S V		0.220	

Table 29

Chi-square Comparison of IVF Cases and Controls on Reactivity

CASECNTL SIS(REACTIVITY)

FREQUENCY / PERCENT / ROW PCT / COL PCT	3	4	5	6	7	8	9	TOTAL
CASE	1	0	2	10	46	2	[illegible]	[illegible]
	0.76	0.00	1.53	7.63	35.11	1.53	[illegible]	[illegible]
	1.59	0.00	3.17	15.87	73.02	3.17	[illegible]	
	100.00	0.00	25.00	35.71	54.12	100.00	[illegible]	
CONTROL	0	3	6	18	39	0	[illegible]	[illegible]
	0.00	2.29	4.58	13.74	29.77	0.00	[illegible]	[illegible]
	0.00	4.41	8.82	26.47	57.35	0.00	[illegible]	
	0.00	100.00	75.00	64.29	45.88	0.00	[illegible]	
TOTAL	1	3	8	28	85	2	4	[illegible]
	0.76	2.29	6.11	21.37	64.89	1.53	[illegible]	[illegible]

STATISTICS FOR TABLE OF CASECNTL BY SIS

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	6	10.687	0.099
LIKELIHOOD RATIO CHI-SQUARE	6	13.115	0.041
MANTEL-HAENSZEL CHI-SQUARE	1	4.292	0.038
PHI		0.286	
CONTINGENCY COEFFICIENT		0.275	
CRAMER'S V		0.286	

Table 30

Chi-square Comparison of IVF Cases and Controls on Sights

CASECNTL SIG(SIGHTS)

FREQUENCY / PERCENT / ROW PCT / COL PCT	2	4	5	6	7	8	9	TOTAL
CASE	1	0	57	2	1	1	1	63
	0.76	0.00	43.51	1.53	0.76	0.76	0.76	48.09
	1.59	0.00	90.48	3.17	1.59	1.59	1.59	
	100.00	0.00	46.72	50.00	100.00	100.00	100.00	
CONTROL	0	1	65	2	0	0	0	68
	0.00	0.76	49.62	1.53	0.00	0.00	0.00	51.91
	0.00	1.47	95.59	2.94	0.00	0.00	0.00	
	0.00	100.00	53.28	50.00	0.00	0.00	0.00	
TOTAL	1	1	122	4	1	1	1	131
	0.76	0.76	93.13	3.05	0.76	0.76	0.76	100.00

STATISTICS FOR TABLE OF CASECNTL BY SIG

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	6	5.342	0.501
LIKELIHOOD RATIO CHI-SQUARE	6	7.266	0.297
MANTEL-HAENSZEL CHI-SQUARE	1	1.265	0.261
PHI		0.202	
CONTINGENCY COEFFICIENT		0.198	
CRAMER'S V		0.202	

Table 31

Chi-square Comparison of IVF Cases and Controls of Listening

CASECNTL SIZ(LISTENS)

FREQUENCY / PERCENT / ROW PCT / COL PCT	4	5	6	7	9	TOTAL
CASE	0	59	2	1	1	63
	0.00	45.04	1.53	0.76	0.76	48.09
	0.00	93.65	3.17	1.59	1.59	
	0.00	49.17	50.00	25.00	100.00	
CONTROL	2	61	2	3	0	68
	1.53	46.56	1.53	2.29	0.00	51.91
	2.94	89.71	2.94	4.41	0.00	
	100.00	50.83	50.00	75.00	0.00	
TOTAL	2	120	4	4	1	131
	1.53	91.60	3.05	3.05	0.76	100.00

STATISTICS FOR TABLE OF CASECNTL BY SIZ

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	4	3.848	0.427
LIKELIHOOD RATIO CHI-SQUARE	4	5.048	0.282
MANTEL-HAENSZEL CHI-SQUARE	1	0.175	0.676
PHI		0.171	
CONTINGENCY COEFFICIENT		0.169	
CRAMER'S V		0.171	

Table 32

Chi-square Comparison of IVF Cases and Controls on Vocalization

CASECNTL SIB(VOCAL SOUNDS)

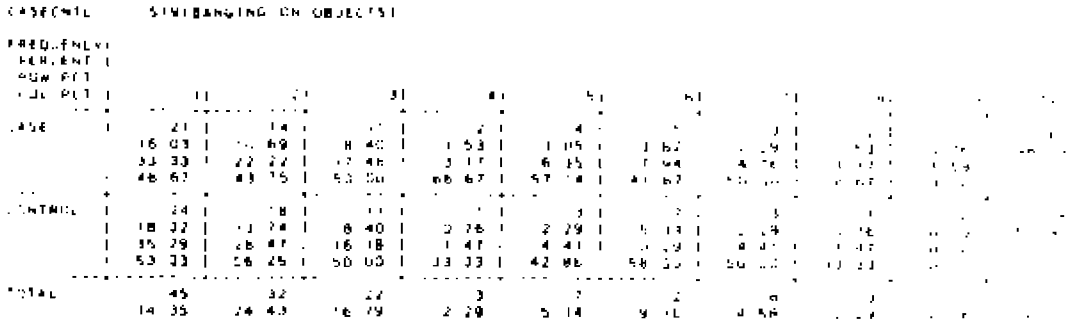
FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	4	5	6	7	8	9	Total
CASE	0	7	17	20	8	1	6	3	1	[illegible]
	0.00	5.34	12.98	15.27	6.11	0.76	4.58	2.29	0.76	48 [illegible]
	0.00	11.11	26.98	31.75	12.70	1.59	9.52	4.76	1.59	
	0.00	46.67	34.69	60.61	44.44	20.00	100.00	100.00	100.00	
CONTROL	1	8	32	13	10	4	0	0	0	[illegible]
	0.76	6.11	24.43	9.92	7.63	3.05	0.00	0.00	0.00	
	1.47	11.76	47.06	19.12	14.71	5.88	0.00	0.00	0.00	
	100.00	53.33	65.31	39.39	55.56	80.00	0.00	0.00	0.00	
TOTAL	1	15	49	33	18	5	6	3	1	[illegible]
	0.76	11.45	37.40	25.19	13.74	3.82	4.58	2.29	0.76	

STATISTICS FOR TABLE OF CASECNTL BY SIB

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	8	59.002	0.015
LIKELIHOOD RATIO CHI-SQUARE	8	23.438	0.003
MANTEL HAENSZEL CHI-SQUARE	1	7.594	0.006
PHI		0.381	
CONTINGENCY COEFFICIENT		0.356	
CRAMER'S V		0.381	

Table 33

Chi-square Comparison of IVF Cases and Controls on Non-vocal sounds



CASECNTL SIVIBANGING ON OBJECTS1

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	4	5	6	7	8	Total
CASE	21	14	7	2	4	1	2	1	45
	16.03	10.69	5.34	1.53	3.05	0.76	1.53	0.76	34.35
	33.33	22.22	11.11	3.17	6.35	1.59	3.17	1.59	
	46.67	43.75	53.85	66.67	57.14	50.00	66.67	50.00	
CONTROL	24	18	6	1	3	1	1	1	55
	18.32	13.74	4.58	0.76	2.29	0.76	0.76	0.76	41.98
	43.64	32.73	10.91	1.82	5.45	1.82	1.82	1.82	
	53.33	56.25	46.15	33.33	42.86	50.00	33.33	50.00	
TOTAL	45	32	13	3	7	2	3	2	131
	34.35	24.43	9.92	2.29	5.34	1.53	2.29	1.53	100.00

STATISTICS FOR TABLE OF CASECNTL BY S1V

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	7	2.656	0.954
LIKELIHOOD RATIO CHI-SQUARE	7	3.055	0.931
MANTEL-HAENSZEL CHI-SQUARE	1	0.524	0.469
PHI		0.142	
CONTINGENCY COEFFICIENT		0.141	
CRAMER'S V		0.142	

Table 34

Chi-square Comparison of IVF Cases and Controls on Manipulation with Hands

CASECNTL S20(MANIPULATE W HANDS)

FREQUENCY / PERCENT / ROW PCT / COL PCT	3	4	5	6	7	8	9	TOTAL
CASE	1	5	49	5	0	2	1	63
	0.76	3.82	37.40	3.82	0.00	1.53	0.76	48.09
	1.59	7.94	77.78	7.94	0.00	3.17	1.59	
	100.00	62.50	44.55	62.50	0.00	100.00	100.00	
CONTROL	0	3	61	3	1	0	0	68
	0.00	2.29	46.56	2.29	0.76	0.00	0.00	51.91
	0.00	4.41	89.71	4.41	1.47	0.00	0.00	
	0.00	37.50	55.45	37.50	100.00	0.00	0.00	
TOTAL	1	8	110	8	1	2	1	131
	0.76	6.11	83.97	6.11	0.76	1.53	0.76	100.00

STATISTICS FOR TABLE OF CASECNTL BY S20

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	6	7.129	0.309
LIKELIHOOD RATIO CHI-SQUARE	6	9.063	0.170
MANTEL-HAENSZEL CHI-SQUARE	1	0.707	0.400
PHI		0.233	
CONTINGENCY COEFFICIENT		0.227	
CRAMER'S V		0.233	

Table 35

Chi-square Comparison of IVF Cases and Controls on Body Motion

CASECNTL S21(BODY MOTION)

FREQUENCY / PERCENT / ROW PCT / COL PCT	2	3	4	5	6	7	8	9	Total
CASE	1	2	5	33	12	5	3	2	[illegible]
	0.76	1.53	3.82	25.19	9.16	3.82	2.29	1.53	[illegible]
	1.59	3.17	7.94	52.38	19.05	7.94	4.76	3.17	
	100.00	28.57	35.71	53.23	38.71	50.00	75.00	100.00	
CONTROL	0	5	9	29	19	5	1	0	[illegible]
	0.00	3.82	6.87	22.14	14.50	3.82	0.76	0.00	[illegible]
	0.00	7.35	13.24	42.65	27.94	7.35	1.47	0.00	
	0.00	71.43	64.29	46.77	61.29	50.00	25.00	0.00	
TOTAL	1	7	14	62	31	10	4	2	[illegible]
	0.76	5.34	10.69	47.33	23.66	7.63	3.05	1.53	[illegible]

STATISTICS FOR TABLE OF CASECNTL BY S21

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	7	8.088	0.325
LIKELIHOOD RATIO CHI-SQUARE	7	9.354	0.228
MANTEL-HAENSZEL CHI-SQUARE	1	1.348	0.246
PHI		0.248	
CONTINGENCY COEFFICIENT		0.241	
CRAMER'S V		0.248	

Table 36

Chi-square Comparison of IVF Cases and Controls on Thumb Sucking

CASECNTL S22(THUMB SUCKING)

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	5	6	7	8	9	Total
CASE	48	5	2	1	1	1	2	1	[illegible]
	38.64	3.82	1.53	0.76	0.76	0.76	1.53	2.29	[illegible]
	76.19	7.94	3.17	1.59	1.59	1.59	3.17	4.76	
	43.24	83.33	50.00	100.00	50.00	100.00	100.00	75.00	
CONTROL	63	1	2	0	1	0	0	1	[illegible]
	48.09	0.76	1.53	0.00	0.76	0.00	0.00	0.76	[illegible]
	92.65	1.47	2.94	0.00	1.47	0.00	0.00	1.47	
	56.76	16.67	50.00	0.00	50.00	0.00	0.00	25.00	
TOTAL	111	6	4	1	2	1	2	4	[illegible]
	84.73	4.58	3.05	0.76	1.53	0.76	1.53	3.05	100.00

STATISTICS FOR TABLE OF CASECNTL BY S22

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	7	9.517	0.218
LIKELIHOOD RATIO CHI-SQUARE	7	11.845	0.104
MANTEL-HAENSZEL CHI-SQUARE	1	5.127	0.024
PHI		0.270	
CONTINGENCY COEFFICIENT		0.260	
CRAMER'S V		0.270	

Table 37

Chi-square Comparison of IVF Cases and Controls on Pacifier Sucking

CASECNTL S23(PACIFIER)

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	5	6	7	8	9	TOTAL
CASE	50	4	2	0	0	2	2	3	[illegible]
	38.17	3.05	1.53	0.00	0.00	1.53	1.53	2.29	48.09
	79.37	6.35	3.17	0.00	0.00	3.17	3.17	4.76	
	46.30	66.67	50.00	0.00	0.00	66.67	66.67	60.00	
CONTROL	58	2	2	1	1	1	1	2	68
	44.27	1.53	1.53	0.76	0.76	0.76	0.76	1.53	51.91
	85.29	2.94	2.94	1.47	1.47	1.47	1.47	2.94	
	53.70	33.33	50.00	100.00	100.00	33.33	33.33	40.00	
TOTAL	108	6	4	1	1	3	3	5	[illegible]
	82.44	4.58	3.05	0.76	0.76	2.29	2.29	3.82	[illegible]

STATISTICS FOR TABLE OF CASECNTL BY S23

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	7	3.941	0.787
LIKELIHOOD RATIO CHI-SQUARE	7	4.735	0.692
MANTEL-HAENSZEL CHI-SQUARE	1	0.570	0.450
PHI		0.173	
CONTINGENCY COEFFICIENT		0.171	
CRAMER'S V		0.173	

Table 38

Chi-square Comparison of IVF Cases and Controls on Toy Sucking

CASECNTL 524(TOYS)

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	4	5	6	7	8	TOTAL
CASE	31	16	3	2	2	1	3	0	[illegible]
	23.66	12.21	2.29	1.53	1.53	0.76	2.29	0.00	[illegible]
	49.21	25.40	4.76	3.17	3.17	1.59	4.76	0.00	[illegible]
	47.69	53.33	30.00	50.00	66.67	50.00	42.86	0.00	[illegible]
CONTROL	34	14	7	2	1	1	4	2	[illegible]
	25.95	10.69	5.34	1.53	0.76	0.76	3.05	1.53	[illegible]
	50.00	20.59	10.29	2.94	1.47	1.47	5.88	2.94	4.41
	52.31	46.67	70.00	50.00	33.33	50.00	57.14	100.00	[illegible]
TOTAL	65	30	10	4	3	2	7	2	[illegible]
	49.62	22.90	7.63	3.05	2.29	1.53	5.34	1.53	[illegible]

STATISTICS FOR TABLE OF CASECNTL BY 524

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	8	4.6043	0.798
LIKELIHOOD RATIO CHI-SQUARE	8	5.488	0.704
MANTEL-HAENSZEL CHI-SQUARE	1	0.004	0.948
PHI		0.189	
CONTINGENCY COEFFICIENT		0.185	
CRAMER'S V		0.189	

Table 39

Chi-square Comparison of IVF Cases and Controls on Energy Level

CASECNTL S25(ENERGY LEVEL)

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	4	5	TOTAL
CASE	0	8	41	10	3	62
	0.00	6.15	31.54	7.69	2.31	47.69
	0.00	12.90	66.13	16.13	4.84	
	0.00	72.73	41.00	66.67	100.00	
CONTROL	1	3	59	5	0	68
	0.77	2.31	45.38	3.85	0.00	52.31
	1.47	4.41	86.76	7.35	0.00	
	100.00	27.27	59.00	33.33	0.00	
TOTAL	1	11	100	15	3	130
	0.77	8.46	76.92	11.54	2.31	100.00

FREQUENCY MISSING = 1

STATISTICS FOR TABLE OF CASECNTL BY S25

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	4	10.926	0.027
LIKELIHOOD RATIO CHI-SQUARE	4	12.583	0.014
MANTEL-HAENSZEL CHI-SQUARE	1	1.678	0.195
PHI		0.290	
CONTINGENCY COEFFICIENT		0.278	
CRAMER'S V		0.290	

Table 40

Chi-square Comparison of IVF Cases and Controls on Gross Muscle Movements

CASECNTL S26(GROSS COORDINATN)

FREQUENCY / PERCENT / ROW PCT / COL PCT	1	2	3	4	5	TOTAL
CASE	1	12	46	7	1	67
	0.77	9.23	35.38	1.54	0.77	47.69
	1.61	19.35	74.19	3.23	1.61	
	33.33	70.59	46.46	20.00	100.00	
CONTROL	2	5	53	8	0	68
	1.54	3.85	40.77	6.15	0.00	52.31
	2.94	7.35	77.94	11.76	0.00	
	66.67	29.41	53.54	80.00	0.00	
TOTAL	3	17	99	10	1	130
	2.31	13.08	76.15	7.69	0.77	100.00

FREQUENCY MISSING = 1

STATISTICS FOR TABLE OF CASECNTL BY S26

STATISTIC	DF	VALUE	PROB
CHI SQUARE	4	8.051	0.090
LIKELIHOOD RATIO CHI-SQUARE	4	8.769	0.067
MANTEL-HAENSZEL CHI-SQUARE	1	2.137	0.144
PHI		0.249	
CONTINGENCY COEFFICIENT		0.241	
CRAMER'S V		0.249	

Table 41

Chi-square Comparison of IVF Cases and Controls on Fine Muscle Movements

CASECNTL S27(FINE COORDINATN)

FREQUENCY / PERCENT / ROW PCT / COL PCT	2	3	4	TOTAL
CASE	5	53	3	61
	3.88	41.09	2.33	47.29
	8.20	86.89	4.92	
	83.33	44.92	60.00	
CONTROL	1	65	2	68
	0.78	50.39	1.55	52.71
	1.47	95.59	2.94	
	16.67	55.08	40.00	
TOTAL	6	118	5	129
	4.65	91.47	3.88	100.00

FREQUENCY MISSING = 2

STATISTICS FOR TABLE OF CASECNTL BY S27

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	2	3.718	0.156
LIKELIHOOD RATIO CHI-SQUARE	2	3.955	0.138
MANTEL-HAENSZEL CHI-SQUARE	1	0.845	0.358
PHI		0.170	
CONTINGENCY COEFFICIENT		0.167	
CRAMER'S V		0.170	

Table 42

Chi-square Comparison of IVF Cases and Controls on Tester's Judgement of Test's Adequacy

CASECNTL S28(JUDGEMENT)

FREQUENCY / PERCENT / ROW PCT / COL PCT	MINIMAL	FAIRLY A DEQUATE	AVERAGE	VERY GOO D	EXCELLEN T	TOTAL
CASE	3	9	14	30	6	62
	2.33	6.98	10.85	23.26	4.65	48.06
	4.84	14.52	22.58	48.39	9.68	
	75.00	50.00	51.85	45.45	42.86	
CONTROL	1	9	13	36	8	67
	0.78	6.98	10.08	27.91	6.20	51.94
	1.49	13.43	19.40	53.73	11.94	
	25.00	50.00	48.15	54.55	57.14	
TOTAL	4	18	27	66	14	129
	3.10	13.95	20.93	51.16	10.85	100.00

FREQUENCY MISSING = 2

STATISTICS FOR TABLE OF CASECNTL BY S28

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	4	3.677	0.795
LIKELIHOOD RATIO CHI-SQUARE	4	3.723	0.787
MANTEL-HAENSZEL CHI-SQUARE	1	1.068	0.301
PHI		0.114	
CONTINGENCY COEFFICIENT		0.113	
CRAMER'S V		0.114	

Table 43

Chi-square Comparison of IVF Cases and Controls on Unusual/Deviant Behavior

CASECNTL S29(DEVIANT BEHAVIOR)

FREQUENCY / PERCENT / ROW PCT / COL PCT	YES	NO	TOTAL
CASE	4	57	61
	3.10	44.19	47.29
	6.56	93.44	
	36.36	48.31	
CONTROL	7	61	68
	5.43	47.29	52.71
	10.29	89.71	
	63.64	51.69	
TOTAL	11	118	129
	8.53	91.47	100.00

FREQUENCY MISSING = 2

STATISTICS FOR TABLE OF CASECNTL BY S29

STATISTIC	DF	VALUE	PROB
CHI-SQUARE	1	0.576	0.448
LIKELIHOOD RATIO CHI-SQUARE	1	0.584	0.445
CONTINUITY ADJ. CHI-SQUARE	1	0.196	0.658
MANTEL-HAENSZEL CHI-SQUARE	1	0.571	0.450
FISHER'S EXACT TEST (1-TAIL)			0.331
(2-TAIL)			0.538
PHI		-0.067	
CONTINGENCY COEFFICIENT		0.067	
CRAMER'S V		-0.067	

Table 44

Chi-square Comparison of IVF Cases and Controls on General Evaluation (Normal versus Exceptional)

CASECNTL S30(GEN. EVALUATION)

FREQUENCY / PERCENT / ROW PCT / COL PCT	NORMAL	TOTAL
CASE	61	61
	47.66	47.66
	100.00	
	47.66	
CONTROL	67	67
	52.34	52.34
	100.00	
	52.34	
TOTAL	128	128
	100.00	100.00

FREQUENCY MISSING = 3

EASTERN VIRGINIA MEDICAL SCHOOL
POST OFFICE BOX 1980
NORFOLK VIRGINIA 23501
TELEPHONE (804) 446-5600

Dear Mr. & Mrs.

We at Eastern Virginia Medical School are very interested in evaluating the growth and development of infants conceived through the in vitro program. We would like very much to see in January. During the visit your child will be evaluated by four pediatric specialists, a clinical psychologist and cranial, cardiac and abdominal ultrasound examinations. We will not be drawing blood or doing any painful procedures. This procedure will require you to visit The Children's Hospital of The King's Daughters in Norfolk for a day.

We will furnish airfares for one parent and infant(s) as well as provide hotel accommodations. We sincerely believe that the information obtained from the visit will benefit your child and will be a comfort to you. Also, it will help prove the validity and safety of the in vitro program. This is an important step in making the in vitro procedure a readily available resource for infertile couples.

We would like to schedule for a visit in January. Within a few days you will be receiving a call from our project secretary, Lelia Gregory, to schedule your appointment and make the necessary arrangements.

Please bring to your appointment the name and address of your current pediatrician so that we may send him results as well as head circumference and dubowitz values at the time of your child's birth.

Sincerely,

Frederick H. Wirth, M.D.
Director, Neonatal Medicine

FHW/lag

EASTERN VIRGINIA MEDICAL SCHOOL
POST OFFICE BOX 1980
NORFOLK VIRGINIA 23501
TELEPHONE (804) [illegible]

Dear Mr. & Mrs.

We at Eastern Virginia Medical School are very interested in evaluating the growth and development of infants conceived through the in vitro program. In order to determine whether there are health risks or benefits from this method of conception, it is important to have a comparison group. Your infant has been randomly selected to participate as a normally conceived child.

Your child's medical examination will be done by four pediatric specialists, a clinical psychologist and cranial, cardiac and abdominal ultrasound examinations. We will not be drawing blood or doing any painful procedures. The examination which normally costs $800.00 will be done at no cost to you at The Children's Hospital of The King's Daughters. It will only take approximately one half of a day.

We sincerely believe that the information obtained from the visit will benefit your child and will be a comfort to you. It will assure you that your child is free of any major malformations if none are found. If malformations are discovered, then the child will benefit from the appropriate therapy started at a very early age.

We would like to schedule as soon as possible. Within a few days you will be receiving a call from our project secretary, Ms. Lelia Gregory, to schedule your appointment for the free medical examination.

Please bring to your appointment the name and address of your current pediatrician so that we may send him results as well as head circumference and dubowitz values at the time of your child's birth.

If you have any additional questions about this study, Dr. Norma Morin can be contacted at (804) 628-7419 or (804) 628-7456.

The success of this project will depend on the support it receives from all the individuals contacted. Therefore, your participation is most important.

Sincerely,

Frederick H. Wirth, M.D.
Director, Neonatal Medicine

FHW/lag

CONSENT FORM

Appendix B

COMPREHENSIVE FOLLOW-UP EVALUATION
OF CHILDREN BORN AFTER INVITRO FERTILIZATION

Name:_____

Chart #:_____

Children's Hospital of the King's Daughters
800 W. Olney Road
Norfolk, Virginia 23507

I understand that I am being asked to give my voluntary consent to an approved research project involving the examination of my child, _____. I understand that the two main reasons for the evaluation of my child are:

1) To assure that there are no detectable defects that might be associated with the process of in vitro fertilization.
2) To allow the physicians at Eastern Virginia Medical School the opportunity to determine the safety of the invitro fertilization process.

I understand that the evaluation will involve the following:
1) psychometric evaluation, using the Bailey's scales, by a child psychologist.
2) a general pediatric evaluation by a neonatologist with special interests in developmental disorders associated with the reproductive process.
3) an evaluation by a pediatric cardiologist and a pediatric neurologist, which involve both a physical examination and an examination using ultrasound to look at the heart and brain anatomy.

At the present time there are no known risks to the use of ultrasound in examining the heart, brain, kidneys, liver and other abdominal organs. Likewise, there are no known risks to the physical exams by the physicians involved in this comprehensive evaluation of my child.

I am advised that if physical injury should result to my child from participation in this study, Eastern Virginia Medical Authority or the Children's Hospital of The King's Daughters provide no insurance coverage, compensation plan, or free medical care plan to compensate me or my child for such injury. In the event I believe my child has suffered physical injury as a result of participation in this study, I may contact Dr. Robert McComms,

COMPREHENSIVE FOLLOW-UP EVALUATION
OF CHILDREN BORN AFTER INVITRO FERTILIZATION

CONSENT FORM PAGE TWO

Associate Dean, Eastern Virginia Medical Authority, telephone number 446-5804. Dr. McCombs will be glad to review the matter with me.

I understand that I have the right to withdraw my child from this project at any time and this withdrawal will not in any way interfere with my child's care in the hospital. If data resulting from this study are published or presented at meetings, my child will not be identified without my written permission.

I have explained the above to the subject on the date stated on this consent form.

Physician's Signature Date

Signature of Parent/Guardian Date

Witness Date

Relationship

IF YOU HAVE ANY QUESTIONS, PLEASE CALL: Dr. Frederick E. Wirth
(804) 628-7419

MEANS FOR MOTHER AGE, MEAN EDUCATION, GESTATIONAL AGE

VARIABLE	LABEL	N	MEAN	STANDARD DEVIATION	MINIMUM VALUE	MAXIMUM VALUE	STD ERROR OF MEAN	SUM	VARIANCE
CASECNTL=CASE									
MOMAGE	MOTHER AGE AT BABY BIRTH	75	34.40000000	3.64283822	27.00000000	42.00000000	0.42063872	2580.00000	13.2702703
MEAN_ED	MEAN PARENT EDUCATION	73	6.86986301	1.50699157	3.50000000	9.00000000	0.17638002	501.50000	2.2710236
GESTATN	GESTATIONAL AGE, WEEKS	87	37.89895470	3.00629120	29.14285714	42.85714286	0.33198932	3107.71429	9.0377867
CASECNTL=CONTROL									
MOMAGE	MOTHER AGE AT BABY BIRTH	88	32.54545455	6.37868053	16.00000000	41.00000000	0.67996963	2864.00000	40.6875653
MEAN_ED	MEAN PARENT EDUCATION	88	7.09659091	1.18868699	4.00000000	9.00000000	0.12671446	624.50000	1.4129768
GESTATN	GESTATIONAL AGE, WEEKS	90	38.56349206	2.43666493	30.42857143	42.57142857	0.25684704	3470.71429	5.9373363

REVISED MDI/PDI: T-TEST FOR DIFFS BETWEEN CASES AND CONTROLS

R E V I S E D T A B L E -- 21 M A R 88

TTEST PROCEDURE

VARIABLE: AGE AGE IN MONTHS

CASECNTL	N	MEAN	STD DEV	STD ERROR	MINIMUM	MAXIMUM	VARIANCES	T	DF	PROB > |T|
CASE	64	17.21875000	6.42531884	0.80316486	10.00000000	29.00000000	UNEQUAL	1.5177	107.3	0.1322
CONTROL	67	15.77611940	4.16631839	0.50899680	9.00000000	29.00000000	EQUAL	1.5315	129.0	0.1281

FOR HO: VARIANCES ARE EQUAL, F'= 2.38 WITH 63 AND 66 DF PROB > F'= 0.0006

VARIABLE: MDI

CASECNTL	N	MEAN	STD DEV	STD ERROR	MINIMUM	MAXIMUM	VARIANCES	T	DF	PROB > |T|
CASE	63	114.96825397	12.70378183	1.60052607	92.00000000	140.00000000	UNEQUAL	1.5614	127.0	0.1209
CONTROL	66	111.37878788	13.10581407	1.65014164	78.00000000	141.00000000	EQUAL	1.5595	127.0	0.1214

FOR HO: VARIANCES ARE EQUAL, F'= 1.11 WITH 65 AND 62 DF PROB > F'= 0.6710

VARIABLE: PDI

CASECNTL	N	MEAN	STD DEV	STD ERROR	MINIMUM	MAXIMUM	VARIANCES	T	DF	PROB > |T|
CASE	63	113.55555556	14.05378812	1.77061087	50.00000000	144.00000000	UNEQUAL	2.0480	126.9	0.0426
CONTROL	66	108.28787879	15.15637987	1.86562140	70.00000000	159.00000000	EQUAL	2.0444	127.0	0.0430

FOR HO: VARIANCES ARE EQUAL, F'= 1.16 WITH 65 AND 62 DF PROB > F'= 0.5505

Appendix E

NORFOLK INFANT STUDY: FREQS OF BIRTH WEIGHT

BWTGM	FREQUENCY	PERCENT	CUMULATIVE FREQUENCY	CUMULATIVE PERCENT
.	10	.	.	.
1105.63	1	0.8	1	0.8
1332.426	2	1.6	3	2.4
1502.523	1	0.8	4	3.2
1559.222	1	0.8	5	4.0
1587.572	1	0.8	6	4.8
1644.271	2	1.6	8	6.5
1672.62	1	0.8	9	7.3
1700.87	1	0.8	10	8.1
1757.669	1	0.8	11	8.9
1856.115	1	0.8	12	9.7
1984.465	1	0.8	13	10.5
2041.164	2	1.6	15	12.1
2069.513	1	0.8	16	12.9
2126.212	1	0.8	17	13.7
2211.261	1	0.8	18	14.5
2267.96	1	0.8	19	15.3
2296.309	2	1.6	21	16.9
2324.659	2	1.6	23	18.5
2353.008	1	0.8	24	19.4
2381.358	1	0.8	25	20.2
2466.406	2	1.6	27	21.8
2494.756	4	3.2	31	25.0
2523.105	2	1.6	33	26.6
2551.455	2	1.6	35	28.2
2608.154	1	0.8	36	29.0
2636.503	2	1.6	38	30.6
2693.202	1	0.8	39	31.5
2721.552	2	1.6	41	33.1
2806.6	2	1.6	43	34.7
2834.95	1	0.8	44	35.5
2849.125	1	0.8	45	36.3
2863.299	1	0.8	46	37.1
2891.649	2	1.6	48	38.7
2919.998	1	0.8	49	39.5
2948.348	4	3.2	53	42.7
2976.697	2	1.6	55	44.4
3005.047	3	2.4	58	46.8
3012.134	1	0.8	59	47.6
3061.746	3	2.4	62	50.0
3090.095	1	0.8	63	50.8
3118.445	1	0.8	64	51.6
3132.62	1	0.8	65	52.4
3146.794	1	0.8	66	53.2
3175.144	1	0.8	67	54.0
3189.319	1	0.8	68	54.8
3203.493	3	2.4	71	57.3
3260.192	1	0.8	72	58.1
3316.891	1	0.8	73	58.9
3345.241	3	2.4	76	61.3
3352.328	1	0.8	77	62.1
3373.59	1	0.8	78	62.9
3401.94	3	2.4	81	65.3
3458.639	2	1.6	83	66.9
3486.988	2	1.6	85	68.5
3515.338	2	1.6	87	70.2
3529.513	1	0.8	88	71.0
3543.687	2	1.6	90	72.6
3572.037	1	0.8	91	73.4
3600.386	2	1.6	93	75.0
3628.736	2	1.6	95	76.6
3657.085	3	2.4	98	79.0
3713.784	3	2.4	101	81.5
3742.134	3	2.4	104	83.9
3798.833	3	2.4	107	86.3
3827.182	2	1.6	109	87.9
3855.532	4	3.2	113	91.1
3883.881	3	2.4	116	93.5
3940.58	1	0.8	117	94.4
3968.93	1	0.8	118	95.2
3997.279	1	0.8	119	96.0
4011.454	1	0.8	120	96.8
4096.503	1	0.8	121	97.6
4139.027	1	0.8	122	98.4
4323.299	1	0.8	123	99.2
4337.473	1	0.8	124	100.0

Appendix F

NORFOLK INFANT STUDY
REVISED: 7 DECEMBER 1987

GESTATIONAL AGE, WEEKS

GESTAIN	FREQUENCY	PERCENT	CUMULATIVE FREQUENCY	CUMULATIVE PERCENT
	3	.		
29.14286	1	0.6	1	0.6
30.42857	6	3.4	7	4.0
31	2	1.1	9	5.2
31.42857	1	0.6	10	5.7
32.42857	2	1.1	12	6.9
34	3	1.7	15	8.6
34.14286	2	1.1	17	9.8
34.42857	3	1.7	20	11.5
34.71429	2	1.1	22	12.6
35.57143	2	1.1	24	13.8
35.71429	5	2.9	29	16.7
36.42857	3	1.7	32	18.4
36.57143	5	2.9	37	21.3
37	5	2.9	42	24.1
37.42857	3	1.7	45	25.9
37.57143	1	0.6	46	26.4
37.71429	4	2.3	50	28.7
37.85714	2	1.1	52	29.9
38	5	2.9	57	32.8
38.14286	2	1.1	59	33.9
38.28571	3	1.7	62	35.6
38.42857	2	1.1	64	36.8
38.57143	11	6.3	75	43.1
38.71429	6	3.4	81	46.6
38.85714	4	2.3	85	48.9
39	9	5.2	94	54.0
39.14286	4	2.3	98	56.3
39.28571	1	0.6	99	56.9
39.42857	3	1.7	102	58.6
39.57143	6	3.4	108	62.1
39.71429	3	1.7	111	63.8
39.85714	5	2.9	116	66.7
40	21	12.1	137	78.7
40.14286	8	4.6	145	83.3
40.28571	5	2.9	150	86.2
40.42857	3	1.7	153	87.9
40.57143	2	1.1	155	89.1
40.71429	3	1.7	158	90.8
40.85714	1	0.6	159	91.4
41	4	2.3	163	93.7
41.14286	2	1.1	165	94.8
41.28571	1	0.6	166	95.4
41.42857	2	1.1	168	96.6
41.57143	2	1.1	170	97.7
41.71429	1	0.6	171	98.3
42	1	0.6	172	98.9
42.57143	1	0.6	173	99.4
42.85714	1	0.6	174	100.0

VITA

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625-1416 (Home)

Experience
Highlights

1981 - present School Psychologist, Children's Hospital of The King's Daughters, 800 West Olney Road, Norfolk, Virginia 2350/

Provide developmental, intellectual, perceptual, academic and emotional assessments for children from one year of age through adolescence, both inpatients and outpatients. Report findings and recommendations to referring physicians, the family, child and other professionals as appropriate. Administer neuropsychological test battery. Provide consultation and liaison services for school placement and rehabilitation requirements. Lecture and supervise graduate psychology students in testing assessment, and school related concerns. Provide clinical rotation for medical students and in-service training for hospital staff. Participate in the development of the Language Disorders/Child Development Clinic within the hospital to provide multidisciplinary assessments and treatment of medical and behavioral problems and in the Neonatal Intensive Care follow up program. Participate on panel with hematologist/oncologist and nurse coordinator to discuss childhood cancer. Participate in research projects involving: in vitro babies and neuropsychological status of leukemia patients.

1976 - 1981 School Psychologist, Virginia Beach Public Schools
Virginia Beach, Virginia

Provided psychological services to elementary, middle and junior high schools, including assessments and recommendations for services. Piloted Child Study Team concept to comply with P.L. 94-142. Cooperated with Instructional Specialists to provide individual programs for students to be mainstreamed. Re-evaluated handicapped students including those placed at the Tidewater Regional Diagnostic and Special Education School. Supervised intern school psychologist from Radford University. Consulted with teachers, administrators, and parents on assorted learning and behavior problems. Communicated findings to school personnel as well as physicians, agencies and other professionals.

1976 School Psychologist, Mt. Lebanon School District
Mt. Lebanon, Pennsylvania

Tested candidates for the gifted program and participated in plans for that program. Helped develop means to comply with P.L. 94-142.

Experience
Highlights (cont.)

1973-1976 School Psychologist, Cuyahoga Falls Public Schools
Cuyahoga Falls, Ohio

Provided psychological services to elementary and junior high schools, including counseling. Provided administrative services for EMR program. Provided testing and placement recommendations for all other handicapping conditions. Filed reports with State Department of Education and other agencies.

1974 School Psychologist (part-time), Akron Psychoeducational Clinic, Akron, Ohio

Provided intellectual, achievement, emotional, perceptual and developmental testing on inpatients at Children's Hospital. Reported findings and recommendations to referring physicians.

1972 - 1973 Intern School Psychologist, Summit County School District, Ohio

License School Psychologist - Issued by Virginia State Board of Psychology, 6/80.

Certificate School Psychologist - Issued by Virginia State Board of Education, 7/86.

Publication "Children and Cancer". (1981). In Grimes, J. and Thomas A. (eds.) Children's Needs: Psychological Perspectives.

Professional Appointments Adjunct Faculty, Department of Psychology, College of William and Mary.

Community faculty member, Department of Psychiatry, Eastern Virginia Medical School

Gifted and Talented Advisory Council, Norfolk Public Schools.

Easter Seals Society Professional Advisory Council, Virginia Beach.

Current Research Participating in In Vitro Follow-up Study sponsored by National Institute of Child Health and Development.

Educational Experience

1983 to Present	Doctoral candidate in Counseling/School Psychology, The College of William and Mary, Williamsburg, Virginia. Degree expected in August 1988.
1971-1973	M.A. in Education, University of Akron, Akron, Ohio. - Specialty: School Psychology.
1967 - 1971	B.A. in Education, The George Washington University, Washington, D.C. - Specialty: Secondary Education.
1981	Training in Halstead - Reitan Neuropsychological Battery at the University of Virginia, Charlottesville, Virginia.
1979	Learning and Motivation, Old Dominion University, Norfolk, Virginia.
1978 - 1980	Counseling Workshops, University of Virginia, Norfolk Extension, Virginia
1977	Elementary School Curriculum, Old Dominion University, Norfolk, Virginia
1975	Reading, Language, and Related Learning Disabilities, Harvard University, Cambridge, Massachusetts.
1974	Educating the Emotionally Disturbed, University of Akron, Akron, Ohio.
1973	School Readiness and Developmental Placement Workshop, Gesell Institute of Child Development, New Haven, Conn.

Presentations

4/88	"In Vitro Babies - How Normal are They?" National Association of School Psychologists Convention, Chicago, Illinois.
5/87	"Emotional Child Abuse" Norfolk Committee for the Prevention of Child Abuse, Norfolk Virginia.
4/86	"Cancer Survivers in Your District" National Association of School Psychologists Convention, Hollywood, Florida

Presentations (cont.)

4/84	"From In-Vitro Toddlers to Leukemia Survivors" National Association of School Psychologist Convention. Philadelphia, Pennsylvania.
3/83	"Leukemia, Neuropsychology, and School Psychology" National Association of School Psychologist Convention. Detroit, Michigan.
4/82	"Emotional Abuse of Children", Children of the 80's Conference, Norfolk, Virginia.
3/82	"School Psychologist as Liaison, Consultant in a Children's Hospital", National Association of School Psychologists Convention, Toronto, Ontario, Canada.

Memberships

National Association of School Psychologists
Virginia Association of School Psychologists
American Orthopsychiatric Association.

Personal Data

Born: 09/18/49
Married to: Malcolm S. Van de Water, Jr.
One son, born 03/24/85
One daughter, born 07/08/86.